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THE CAUSATION OF INTRACRANIAL HEMORRHAGES IN THE NEW-BORN *

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An understanding of the causation of intracranial birth hemorrhages, while admittedly important for diagnosis and treatment, is essential for the far more urgent problem of their prevention. Under prevailing conditions, the task of diagnosis and treatment in the main rests with pediatrician and surgeon. The question of prophylaxis, for evident reasons, concerns most of all the obstetrician.

This relative difference of interest in the problem of intracranial birth trauma on the part of the obstetrician, on the one hand, and the pediatrician on the other, finds its expression in the extensive literature of the past decade on this subject. Obstetricians, naturally, have the better opportunity of observing and studying the immediate and especially the mechanical causes of such injuries. They apparently have succeeded in revealing the exact mechanism in the origin of most of the more common types of cranial and intracranial lesions sustained by the child in the course of birth. Pediatricians, who with the rarest exceptions see these patients only later, have made valuable contributions, chiefly in regard to symptomatology. They have discovered the evident etiologic relation of intracephalic birth hemorrhages to a reduced coagulability of the blood, rather frequently ascertainable in the newborn. But, in my belief, pediatricians and surgeons at present greatly overrate the rôle played by hemorrhagic diathesis in the etiology of these hemorrhages. There is danger, I fear, that a wider acceptance of this idea might impair the efforts of obstetricians in regard to the prevention of these lesions.

It is the purpose of this paper to present from the standpoint of the obstetrician the question of the causation of all types of intracranial birth injuries, which, it must be remembered, are not necessarily hemorrhages.

On a previous occasion [1] I had an opportunity to describe in detail a certain confusion of ideas in literature concerning the actual factors

* Received for publication, Aug. 2, 1923.

1. Ehrenfest, Hugo: Birth Injuries of the Child, New York, D. Appleton & Co., 1922.

responsible for injuries of intracranial structures during birth. Their frequent association with external traumatic lesions, their anatomic characteristics and their location, at first brought mechanical factors as the direct and immediate cause of their production into the foreground. The normal physiologic reduction of the intracranial space during molding, but especially forced and exaggerated compression in the cases of mechanical dystocia or of operative delivery (forceps and breech extraction), seemed most obviously to represent the mechanical factors responsible for the intracephalic traumatization. Further observations, however, and especially necropsy studies since the introduction of Beneke's method of opening the skull, revealed the fact, now generally accepted, that extensive destruction of structures frequently occurs also within the skulls of infants born spontaneously after easy and quick labors, and even in children delivered by cesarean section. An explanation of the intracranial trauma on the basis of mechanical influences, at least for such cases, seemed unsatisfactory. Thus, writers began to add as causative factors prematurity, syphilis, asphyxiation, and more recently, hemorrhagic diathesis. It can be admitted that possibly all of these factors in some form may enter into the etiology of the various types of intracranial birth lesions, and especially of birth hemorrhages; but more careful analysis leads to the inevitable conclusion that, in the individual case, they vary greatly among themselves in significance.

Various attempts have been made to group the cases of intracranial hemorrhage in the new-born in accordance with the supposed predominant etiologic factor. It was thought that such a division would prove of practical value for the purpose of diagnosis and treatment.

Warwick [2] proposed the following classification:

1. Traumatic cases, the result of the molding of the head in normal precipitate deliveries.

2. Congestion of stasis, with rupture of veins, in protracted or complicated labors.

3. A diseased condition of the child in intrauterine life, having no relationship to labor as such.

Warwick thought that the first division, theoretically at least, would represent the most common cause of injuries. In the second group, congestion and overdistension of veins lead directly to hemorrhage or indirectly to rapid degeneration and subsequent rupture. In the third group, the hemorrhagic disease of the new-born naturally would deserve first place.

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2. Warwick, M.: Cerebral Hemorrhage of the New-Born, Am. J. M. Sc. **158**:95 (July) 1919.

Munro and Eustis [3] accepted this division as essentially correct, but felt that asphyxia as a cause for congestion and stasis with rupture of the cerebral veins is sufficiently important to demand special consideration. They, therefore, modified Warwick's classification thus:

1. Traumatic group: hemorrhage caused by excessive molding of the head and overriding of the sutures.

2. Asphyxia group: hemorrhage caused by excessive cerebral venous congestion with rise of intracranial pressure.

3. Fetal disease group: hemorrhage having no relation to the labor, but being most commonly caused by hemorrhagic disease and rarely by syphilis or other toxemias.

Since grouping clinical asphyxia, "an easily diagnosed condition," separately in their etiologic classification, Munro and Eustis have found that the number of cases of intracranial hemorrhage which might be properly classed as traumatic in origin has become relatively quite small. Almost as an apology for still maintaining the traumatic group in their classification, they add: "Nevertheless, as long as fracture of the skull occurs, and as long as there continues to be a tearing of the sinuses and meninges by excessive overlapping of the sutures, so long will it be necessary to classify certain of these cases as strictly traumatic in origin."

Such a statement, if accepted as correct by pediatricians, will go far in obscuring what already has been revealed by the investigations of obstetricians concerning the traumatization of intracephalic structures incident to the process of birth.

At the outset, I wish to emphasize a striking difference in the points of view of pediatrician and obstetrician. The pediatrician tends to adhere to the erroneous belief that the terms intracranial birth hemorrhage and birth injury are synonyms. This evidently is due to the fact that he sees and, therefore, becomes interested only in injuries associated with hemorrhage, the latter alone causing symptoms evident immediately after birth. The obstetrician, from the standpoint of prophylaxis, is concerned with lesions without hemorrhage as well as with those associated with extravasation of blood.

There are a few facts concerning intracranial birth lesions which may be regarded as established beyond all reasonable doubt. Among them, as bearing more specifically on the problem under discussion, I shall mention the following: In necropsies properly performed on all stillborn infants and on new-born infants dying within the first few days of life, some lesion, clearly traumatic in origin, is discovered within the skull in approximately one half of the cases. Most common among

3. Munro, Donald, and Eustis, R. S.: Diagnosis and Treatment of Intracranial Hemorrhage in the New-Born, Am. J. Dis. Child. **24**:273 (Oct.) 1922.

them are tears of the tentorium. In a considerable number of the cases, estimated at from 20 to 25 per cent., the intracephalic injury is not directly responsible for the death but represents merely an incidental finding. In these instances, as a rule, the lesion is accompanied by only a negligible hemorrhage or none at all. Necropsies on somewhat older infants, dying from intercurrent diseases, often reveal the remnants or evident sequelae of hemorrhages which undeniably have occurred at the time of birth. In the larger number of instances in this latter group, the history fails to show any symptoms in the new-born which would have suggested an intracranial traumatization.

From these facts, we can draw at least two definite conclusions: (1) that not all intracranial birth lesions cause death or even marked symptoms in the new-born, and (2) that intracephalic injuries, sustained in birth, must occur with even greater frequency than is indicated by the postmortem findings in new-born infants.

Observations and experimental studies, extensively recorded in the literature of obstetrics, have now determined the exact mechanical factors which effect the traumatization of the meninges, especially of the dura mater.

Compression of the fetal head, resulting in a relatively small reduction of the volume of the skull, but leading to a rather marked change in its configuration, represents an integral element of every labor. Experience proves that, in general, this compression is free of any noteworthy harmful effect on the child. Under normal conditions, a process is at work which precludes a pathologic increase of intracranial pressure. As now understood, this protection of the skull contents and, most important, of the brain tissue, is procured by the escape of a small amount of cerebrospinal fluid toward the spinal canal, and furthermore by a reduction of the volume of blood within the brain.

The process of molding effects a change in the relative position of adjoining skull bones which is most pronounced in the sagittal suture. As the result of the overriding of the parietal bones, the subjacent dura is both folded and stretched. If this overlapping is excessive (mechanical dystocia) or is very suddenly accomplished (forceps extraction, large doses of pituitary extract), or if the dura is abnormally fragile (prematurity), the strained dura may break. The longitudinal sinus itself may be torn open or, as is more commonly the case, the tear may involve only the veins on one side, exactly at the site of their entrance into the sinus. If these vessels are engorged (asphyxiation, or passive congestion in the aftercoming head), they naturally will break under a relatively smaller strain. Under these conditions, obviously, the resulting hemorrhage will be more profuse. If, coincidentally, there is an abnormal delay in the blood clotting

(hemorrhagic diathesis), the hemorrhage will continue, and may attain dangerous proportions, even if the tear is small and involves but a few, and those small, vessels.

In a breech extraction not properly managed, exaggerated lapping of the parietals over the squama of the occipital bone in an identical manner may cause the rupture of veins emptying into the transverse sinus, or laceration of the sinus itself, or might push the cerebellum with sufficient force against the overlying tentorium to cause its laceration.

Far more significant, however, than this overlapping of adjoining skullbones is the changed configuration of the molded head in the direct mechanical causation of meningeal lacerations. The exact mechanism of the traumatization of the tentorium, the almost typical and indeed most common form of birth injury, has been definitely established by the pioneer work of Beneke.[4] It has been fully confirmed by many other investigators, among them Eardley Holland[5] and Capon.[6] I refer readers interested in the details of the problem to my monograph,[1] or to the papers of Holland and Capon, and I wish to emphasize in this connection that the mechanical conditions leading to tentorial laceration can easily be reproduced and demonstrated on the head of a new-born infant, opened at necropsy in accordance with Beneke's suggestion (Figs. 1, 3, 4).

Compression of the head in any one direction results in the shortening of the diameter lying in the direction of the pressure, and a simultaneous compensatory lengthening of the diameter perpendicular to the one reduced. Therefore, compression of the head, during the second stage of labor, along either the anteroposterior or the lateral diameters, always leads to an increase in the length of the vertical diameters of the infant's head. The cranium becomes more convex and the falx is pulled upward. It is generally believed that certain histologic structural details of such tissues as bones or ligaments permit reliable deductions in regard to the functional purpose of these textures. The longitudinal arrangement of the fibers in the falx and their lateral extension on either side into the tentorium then would indicate that it is the chief mechanical task of the falx to prevent an abnormal extension of the long diameters of the cranium; i. e., to counteract during molding the effect of lateral compression. But sudden or excessive compression in either a lateral or a longitudinal direction, by raising the

4. Beneke: Ueber Tentoriumzerreissung bei der Geburt, etc., München. med. Wchnschr. **57**:2125, 1910.

5. Holland: Cranial Stress of the Foetus During Labor, J. Obst. & Gynec. Brit. Emp. **29**:551, 1922.

6. Capon, N. B.: Intracranial Traumata in the New-Born, J. Obst. & Gynec. Brit. Emp. **29**:572, 1922.

falx, would exert a definite pull at the place where the fibers of the falx diverge to either side to form the upper blade of the tentorium. This also represents the relatively weakest part of the falx and, as a matter of fact, it is the site of predilection for tentorial tears.

Three specimens, recently obtained in the service of the obstetric department of Washington University, clearly show various points of interest and importance.

In Figure 1, the head of a small fetus, the structure of the anterior part of the falx well expresses its vulnerability. The tentorial blades are so thin that the underlying cerebellum can be seen through them. Who will doubt that these thin dura folds might easily be torn, if this

Fig 1.—Head of small fetus showing the thinness and vulnerability of falx and tentoria. Through the latter the outline of the underlying cerebellum can be seen. The fibers of the falx diverge posteriorly on either side into the upper blade of the tentorium. The head was opened after the Beneke method.

head by a strong uterine contraction (perhaps induced by pituitary extract) was quickly forced through a not fully dilated cervix or through the rigid vulvar ring of a primipara? The softness and elasticity of the cranial bones of a premature fetus favor exaggerated change in configuration and thus increase the danger to the fragile dura. This assumption is well supported by a comparison with the observations made in the next case.

The specimen was obtained by the department from an outside physician. A futile attempt had been made to extract a very large,

Fig. 2.—Head of a postmature fetus. The right parietal bone was fractured in an attempt at extraction by means of high forceps.

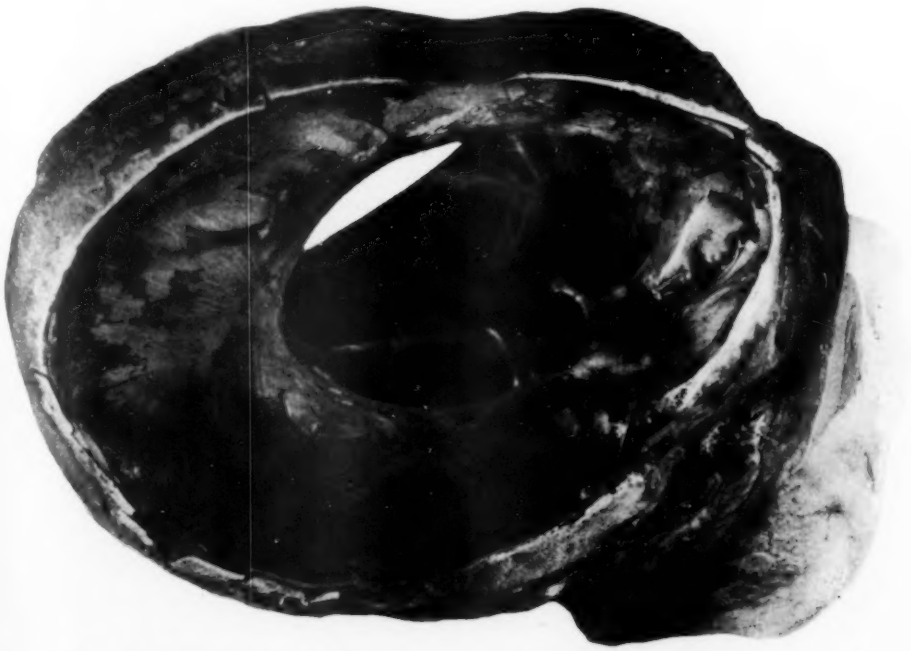

Fig. 3.—Same head as in Figure 2, showing the interior. The dura is intact. Hemorrhages between the blades of the falx can be seen.

clearly overcarried infant, by means of a high forceps. The results can be seen in Figures 2 and 3. External force proved sufficient to cause deep fractures of both parietal bones (only the right parietal is shown in Fig. 2). The hard skull bones, however, proved too rigid to permit a marked change in the configuration. Falx and both tentoria remained intact, exhibiting the effect of the very severe trauma solely in the form of small hemorrhages confined between the dura blades (Fig. 3).

Fig. 4.—Head of full term infant, stillborn spontaneously in vertex presentation. Both tentoria are torn, the right more extensively. There is a hole in the falx, leaving the vessels crossing the opening intact. There are three distinct traumatic lesions, of which only two caused hemorrhage.

In the third skull (Fig. 4), that of a stillborn infant, spontaneously expelled, head first, the skull bones remained intact, but there was found a deep tear of the right tentorium, severing both blades, another tear through the left tentorium and an opening in the falx. This last injury is particularly instructive. While the dura tissue itself was found split, the vessels running through this area remained intact, as

can be seen in the illustration. Thus, this particular opening in the falx represents an intracranial traumatic birth injury causing no hemorrhage.

An appreciation of the direct mechanical causes of tentorial tears, as already described and convincingly demonstrated in the few specimens illustrated here, would seem to render entirely acceptable the assertion of some authors, that meningeal injuries may be the result of unskilful manipulations during resuscitation; e. g., of too firm a fixation of the infant's head between the wrists during swinging after Schultze's method; or that they might be produced near the end of the second stage of a normal and spontaneous labor, when the attendant presses the occiput of the fully rotated head too forcibly toward the symphysis in an effort to protect the perineum against injury. Serious intracranial hemorrhages have been recorded in infants delivered by cesarean sections. In some of these cases, the traumatization undeniably occurred before operation as the result of the effort of the uterus to force the relatively too large fetal head into the narrowed pelvic inlet. In other instances, in which operation was actually performed before the onset of labor, the infant's head evidently was severely traumatized solely by its forced extraction through a uterine incision of insufficient length.

The obstetrician, thoroughly familar with such facts, must disagree with Monro and Eustis that intracranial birth hemorrhages are but rarely traumatic in origin.

These authors proclaim asphyxiation as the most common etiologic factor in such hemorrhages. They write:

> At birth, clinically asphyxiated babies are cyanotic, do not start breathing well, or cry, and require treatment which is directed toward the artificial stimulation of respiration. It has also been repeatedly observed that these clinically asphyxiated babies, when they die, die from respiratory failure, the heart continuing to beat for some time after the respiratory center has definitely ceased to function, and after it will no longer react to artificial stimulation. Until this clinical evidence can be disproved by chemical studies of the blood of the new-born infant, therefore, we must consider the baby exhibiting the above symptoms as asphyxiated.

One cannot resist the temptation to add: "If there is no necropsy in such a case, the diagnosis asphyxia will be given as the cause of death in the death certificate; but if there is a necropsy, in the overwhelming majority of these cases an intracranial hemorrhage will be found; and the cause of death should have been given as traumatic intracranial birth injury." In all cases of severe birth hemorrhage, the baby, if born alive, is asphyxiated. I maintain that every baby born seemingly asphyxiated should be considered as possibly suffering from an intracranial traumatization, and, therefore, should not be subjected to any violent efforts at resuscitation, because such manipulations might

in themselves aggravate the hemorrhage just enough to cause the death of the infant. It is unfortunate that we are unable to differentiate in the new-born a true asphyxia, the result of mechanical interference with oxygen supply, from the clinical picture of asphyxiation, brought on by the traumatization of the breathing center.

The undisputed fact that the overwhelming majority of babies, found at postmortem to have succumbed to an intracephalic hemorrhage, after birth were cyanotic and did not breathe properly, cannot be adduced as proof of the great importance of asphyxia as the direct cause of such hemorrhages. Of no more value in this respect is the often emphasized fact that small petechial hemorrhages, generally considered as characteristic of asphyxiation, are found in the various serosae of these infants. This is not surprising since these babies died in a state of asphyxiation resulting from the improper function of the breathing center. The one question under discussion is whether the asphyxia is responsible for the intracranial hemorrhage, or the intracranial hemorrhage for the asphyxia. I am not aware of the fact that asphyxiation in young children commonly, if ever, causes the rupture of meningeal veins or of a large sinus merely from overdistention. It then seems unreasonable to insist on this particular mechanism for the rupture of intracranial vessels in the course of birth simply on theoretical grounds, with the added necessity of disregarding deliberately the factor of the compression of the head, a factor unquestionably of a traumatic nature and present in the second stage of every labor. However, it can be readily admitted that a passively congested vein or sinus of a deeply asphyxiated infant is more liable to rupture under external pressure or strain.

The effect of a meningeal tear on the infant in the main is determined by the hemorrhage resulting from it. The occurrence of a hemorrhage and the size of the hematoma, therefore, actually depend on whether any vessels are torn and whether they are small or large, empty or full. Thus, asphyxiation enters into the problem of intracranial birth hemorrhages, but only as a predisposing and contributory cause, and not as the direct cause of the injury. Asphyxiation positively cannot have any bearing on the fact that so often in labor the tentorium is torn.

As a third etiologic factor, Warwick, Munro and Eustis and many others emphasize hemorrhagic diathesis. It is impossible to establish any immediate relation between this disease and lacerations of the dura mater *per se*. While this anomaly of the blood undeniably is responsible for certain fairly common types of hemorrhage from various mucosae of the new-born, I cannot see how it could be adduced as an acceptable explanation of hemorrhages evidently resulting from the rupture of a sinus or vein within the skull, again with utter dis-

regard of the mechanical factor of compression of the head during the process of molding. Nevertheless, it must be admitted that hemorrhagic diathesis also plays some rôle in the etiology of intracranial birth hemorrhages, even more important than asphyxia, but again only as a contributory factor. If the blood coagulation time is greatly increased, the unduly prolonged extravasation of blood even from a very small vessel will finally prove as disastrous as the rupture of a large vessel in another infant with normal coagulation time. The very gradual formation of the hematoma under these conditions explains the not uncommon appearance of the first manifest symptoms of an intracranial injury only some time after birth.

I should like to call attention in this connection to the seemingly conclusive experiments and investigations of Evarts A. Graham [7] concerning the pathogenesis of the hemorrhagic diseases. He established the fact that all those conditions of the new-born which are characterized by a hemorrhagic tendency most probably are the result of a deficiency in oxidation, and can be experimentally produced by chloroform as well as by direct asphyxiation. These, indeed, are findings of far-reaching importance in clearing up some of the obscurer points in the etiology of intracranial birth hemorrhages and their relation to asphyxiation and hemorrhagic diathesis.

Syphilis and the toxemias of pregnancy, which are cited as direct causes of birth hemorrhages, can be accepted only as predisposing factors. Any disease which tends to lead to the premature termination of pregnancy is of etiologic significance because all structures of the immature fetus, and especially those within the skull, admittedly are very fragile and vulnerable. As far as the toxemias are concerned, the fact furthermore must be borne in mind that they frequently call for the termination of labor by artificial and forcible means, which notoriously augment the direct mechanical dangers to the fetal head.

In the light of our present information, it seems best to differentiate accurately between the *direct mechanical* and the *predisposing* and *contributary factors* in the causation of intracranial birth injuries in general, and of birth hemorrhages in particular. The etiology of intracranial injuries sustained in birth might be described briefly thus: The meninges and the brain substance itself might be traumatized by severely injured skull bones (indentations, depressed fractures). More often, in the absence of any evidence of an external injury, a dura fold is torn as the result of a severe strain if molding is excessive or suddenly accomplished. Such mechanical traumatization of the meninges, therefore, most often is observed in difficult labors and those terminated artificially. But the physiologic trauma also, incident

7. Graham, E. A.: Pathogenesis of the Hemorrhagic Diseases of the New-Born, J. Exper. Med. **15**:307, 1912.

to a spontaneous and seemingly normal birth, might be sufficient to cause the laceration of parts of the dura mater and, with them, of a sinus or veins, in the presence of such predisposing factors as prematurity or marked congestion. Contributory factors in the formation of the hematoma are congestion and hemorrhagic disease, more indirectly also certain reprehensible methods of resuscitation of the seemingly asphyxiated new-born infant.

A grouping of the various etiologic causes of intracranial birth injuries in this manner does not in the least detract from its value as an aid in diagnosis or treatment, but unquestionably is of greater advantage in the more important problem of their prevention.

Emphasis properly belongs on those primarily mechanical factors which cause intracranial structures to be crushed or torn, with more or less hemorrhage resulting from the injuries. The frequency with which such injuries involve more than one structure within the cranium (e. g., both tentoria and falx in the case shown in Fig. 4) well accounts for the perplexing symptomatology and the futility of surgical interference in many of the cases.

Metropolitan Building.

THE DEVELOPMENTAL TOPOGRAPHY OF THE LARYNX, TRACHEA AND LUNGS IN THE FETUS, NEW-BORN, INFANT AND CHILD*

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The development of the respiratory system in the embryonic period of man has been carefully worked out by a number of observers and the features of the process are well known. On the other hand, the development of this system from the third fetal month to birth, in early infancy, later infancy and childhood has received little attention. The present report is a study of the topographic relationships of the larynx, trachea and lungs, with especial emphasis on the changes in this relationship during the entire developmental period. All the available data on the subject, for infancy, childhood and adult life, have been correlated with my findings in the fetus, the new-born infant and the child. It is hoped that in this way a picture may be sketched of the relation of the parts of the respiratory system to the vertebral column, beginning with early fetal life and ending with maturity.

A few observations in addition to those mentioned above have also been made and recorded. These include the lobation of the lungs, the development of the cardiac notch, the angle that each bronchus makes with the midsagittal plane and the relation of the apices of the lungs to the suprasternal notch. A study of the lineal growth of the component parts of the respiratory system was also made in conjunction with the present paper, but the results of that study will be reported separately.

MATERIAL AND METHODS OF COLLECTING DATA

The material used in this study consisted of 102 fetuses and full-term new-born children, ranging in crown-heel or total body length from 10 to 55 cm.; midsagittal sections of a 5 year and an 8 year old child; a model of the topography of the thoracic and abdominal viscera of a 65 mm. human embryo, and a series of tracings of medially sectioned human fetuses. The major part of the material forms part of the collection of the Institute of Anatomy of the University of Minnesota; the remainder is part of the collection of the Department of Anatomy of the Medical College of Virginia. Eighty-two of the fetuses were still-born and twenty-two were infants in whom respiration had been partially established, as indicated by the condition of the lungs. The fetuses and full-term infants were preserved by intravascular injection of an

* Received for publication, Sept. 10, 1923.

* From the departments of anatomy of the University of Minnesota and of the Medical College of Virginia.

aqueous solution of 10 per cent. formaldehyd and 1 per cent. chromic acid. No material in which pathologic conditions were macroscopically observable was used in this study.

The material was prepared in the following manner:

The skin, muscles, etc., were dissected from the anterior of the neck and thorax; the clavicles and costal cartilages were cut along the anterior axillary line, and the anterior part of the thoracic cage was then removed. The infrahyoid muscles, thyroid gland, thymus, heart and great vessels were next carefully dissected out, leaving the larynx, trachea, bronchi and lungs fully exposed in situ. The chin was always held in a horizontal position in order to avoid elevation or depression of the larynx and trachea due to over-extension or depression of the head.

The thyrohyoid membrane was next cut in order to make visible the tip of the epiglottis, which was taken as the superior limit of the larynx. A pin was then inserted into the vertebral column to mark the level of the tip of the epiglottis. The inferior vertebral level of the larynx was marked by a pin at the level of the inferior margin of the cricoid cartilage. A pin was inserted into the vertebral column on each side at the apex of each lung in order to determine its uppermost level. Pins were similarly placed at the most inferior level of each lung. Later, when the heart was removed, the vertebral level of the tracheal bifurcation was marked by a pin inserted into the vertebral column.

The following observations were made and recorded from each individual:

1. Crown-heel length, or total body length, from the vertex of the head to the base of the heel.
2. Crown-rump length, or sitting height, from the vertex of the head to the tip of the coccyx.
3. Vertebral level of the tip of the epiglottis.
4. Vertebral level of the inferior margin of the cricoid cartilage.
5. Vertebral level of the bifurcation of the trachea.
6. Relation of the apices of the lungs to the suprasternal notch.
7. Vertebral level of the apex of the right lung.
8. Vertebral level of the apex of the left lung.
9. Vertebral level of the most inferior part of the inferior margin of the right lung.
10. Vertebral level of the most inferior part of the inferior margin of the left lung.
11. Angle formed by the right bronchus with the midsagittal line.
12. Angle formed by the left bronchus with the midsagittal line.
13. Number of lobes and irregularities of fissures in the right lung.
14. Number of lobes and irregularities of fissure in the left lung.
15. Greatest depth of the cardiac notch.

In order to determine the vertebral levels of the several structures and organs, the vertebral column was split in its midline and the levels of the insertions of the pins were observed and recorded.

THE LITERATURE

The changes in topography of different parts of the human respiratory system in the developmental period have received considerable attention from several investigators, although apparently all the levels here presented have not been considered together in any single study in the past. The relation between the trachea, lungs, thymus and heart in fetal life and in the new-born was discussed in a previous paper.[1] There are several illustrations in the literature of midsagittal sections of fetuses [2] and new-born infants,[3] from which the laryngeal levels may be obtained. All of these which I have found have been plotted against total body length as was done in my own cases. These are shown in Figure 4, along with the data in the literature for these levels obtainable for infancy,[4] childhood,[5] and adult life.[6]

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1. Noback, G. J.: A Contribution to the Topographic Anatomy of the Thymus Gland, with Particular Reference to Its Changes at Birth and in the Period of the New-Born, Am. J. Dis. Child. **12**:120 (Aug.) 1921.

2. Ballantyne, J. W.: An Introduction to the Diseases of Infancy, Edinburgh, 1891, pp. 56-57. Cheivitz, J. H.: A Research on the Topographical Anatomy of the Full-Term Human Fetus in Situ, Copenhagen, 1899, pp. 14-16. Keibel and Mall: Human Embryology, Philadelphia, 1910, Vol. 2, p. 402, Mehnert, E.: Ueber Topographische Altersveränderungen des Atmungsapparats, Jena, 1901. Merkel, F.: Menschliche Embryonen verschiedenen Alters auf Medianschnitten untersucht, Göttingen, 1894. Scammon, R. E.: Private collection, University of Minnesota Department of Anatomy. Symington, J.: On the Relation of the Larynx and Trachea to the Vertebral Column in the Fetus and Child, Edinburgh M. J. **26**:913, 1881.

3. Birkenbusch: Die inneren Proportionen des menschlichen Halses in den verschiedenen Lebensaltern, Dissertation, Göttingen, 1890. Jackson, C. M.: On the Developmental Topography of the Thoracic and Abdominal Viscera, Anat. Rec. **3**:361, 1909. Merkel, F.: Handbuch der topographischen Anatomie, Braunschweig, 1899, Vol. 2, p. 405 (Fig. 70). Mettenheimer, H.: Ein Beitrag zur topographischen Anatomie der Brust Bauch und Beckenhöhle des neugeborenen Kindes., Morph. Arbeiten **3**:301, 1893. Piersol, G. A.: Human Anatomy, Philadelphia 1908, p. 1828. Ribemont, A.: Recherches sur l'anatomie topographique du fetus, 1878, Thèse, Paris, No. 203. Rudinger, F.: Topographisch-chirurgische Anatomie des menschen, Atlas, Stuttgart, 1873, Plate 4, Figure a.

4. Engel, St.: Form, Lage und Lageveränderungen des Bronchialbaumes im Kindesalter, Arch. f. Kinderh. (Festschrift f. Baginsky) **60-61**:267, 1913. Jackson, C. M.: Private collection, University of Minnesota Department of Anatomy. Symington, J.: The Topographical Anatomy of the Child, Edinburgh, 1887, (Plates 1 and 2).

5. Dwight, T.: Frozen Sections of a Child, New York, 1881, p. 15, Plate 3. Gedgowd, V. A.: Anatomical Peculiarities of the Respiratory Organs in Children, Dissertation, St. Petersburg, 1900, pp. 178, Plate 1 (Russian). Sluka, E.: Ueber Roentgenbefunde bei tuberculösen Kindern mit expiratorischen Keuchen, Wien. klin. Wchnschr. **23**:156, 1910. Zuckerkandl, E.: Atlas der topographischen Anatomie des Menschen, 1899, p. 163, Figure 170.

6. Corning, H. K.: Lehrbuch der topographischen Anatomie, Ed. 10 and 12, Munich and Wiesbaden, 1920, p. 202, Figure 164. Cunningham: Textbook of Anatomy, Ed. 4, 1913, p. 1077. Gray-Lewis: Anatomy of the Human Body, 1920, Philadelphia, p. 1084. Hyrtl, J.: Lehrbuch der Anatomie des Menschen,

(Footnote 6 continued on next page)

The most comprehensive study of the topographical changes of the human respiratory system is that of Mehnert (1901).[7] His study includes the literature on the subject up to that time, not only for fetal life but also for all stages through senility in postnatal life. The prenatal material which he personally studied was somewhat limited in that the epiglottis was not considered and that his cases of fetuses and new-born infants numbered only ten in addition to seven cases of Merkel and one case of Disse, or a total of eighteen. He considered the following levels: cricoid cartilage, tracheal bifurcation and the inferior margin of the lungs; all of which, with the addition of the epiglottis and the superior limit of the lungs in relation to the sternal notch and to the vertebral column, were also utilized in the present study.

Mehnert concludes that there is a definite descent with age, but states that the fetal cricoid level is similar to that in the new-born. He finds marked variation in the fetal levels of the cricoid and states that this level shows no marked tendency upward or downward but rather an oscillation. This, he believes, may be partly due to the varying position of the heads in the different cases studied, but he says that the differences in this level should be regarded as individual variations. The level of the inferior margin of the cricoid cartilage in the new-born also varies markedly according to the data of several other investigators and the one case of his own.

Mehnert's conclusions regarding the vertebral level of the tracheal bifurcation are similar to those regarding the level of the larynx. Here, again, he had ten cases of his own and seven cases of other investigators. He states that there are as great variations in this level in some fetal months as are found in his whole series, and that therefore the wide fluctuations should be regarded as individual variations. The level of the bifurcation in the trachea in the new-born he finds to be lower than that in the fetus. The explanation of this, he believes, lies in the fact that, in the fetus, the trachea is craniad to the viscera; whereas, in the new-born,

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Wien, 1889. Joessel, J.: Lehrbuch der topographischen chirurgischen Anatomie, Bonn, Ed. 2, 1899. Luschka, H.: Die Anatomie der Brust des Menschen, Tübingen, 1863, p. 463. Morris-Jackson: Text-Book of Human Anatomy, Ed. 6, Philadelphia, 1921, p. 1254. Potter, Peter: Topography of the Thorax and Abdomen, University of Missouri Studies, Science Series, Vol. 1, No. 1, Columbia, Mo., 1905. Poirer et Charpey: Traité d'anatomie humaine, Paris, 1901, Vol. 3, p. 402 and Figure 203. Quain's Elements of Human Anatomy, London, 1914, Vol. 2, Part 2, p. 152. Rauber-Kopsch: Lehrbuch der Anatomie, Leipzig, 1911, Ed. 9, No. 4, p. 190. Spalteholz, W.: Atlas der Anatomie des Menschen, Leipzig, 1920, p. 480, Figure 516. Testut, L.: Traité d'anatomie humaine, Paris, 1911, Vol. 3, p. 763, Figure 676. Testut et Jacob: Traité d'anatomie topographique, Paris, 1909, p. 629. Toldt, C.: Anatomischer Atlas, Ed. 6, Vol. 4, p. 483, Figure 813.

7. Mehnert: Footnote 2, fourth reference.

it is caudad, and therefore has the weight of the viscera pulling it downward.

According to Mehnert, the level of the larynx and of the tracheal bifurcation show no definite descent during prenatal life, but between early fetal life and maturity there is a descent in these levels of a distance represented by five vertebrae. The inferior margins of the lungs in this period of time also undergo a descent which he measures by two intercostal spaces.

Jackson,[8] in whose private collection are a number of drawings of midsagittal sections of specimens in the Leipsic Museum, furnishes levels of the epiglottis and larynx of the two new-born infants and of a 2-day-old child.

Merkel (1894)[9] illustrates and describes several embryos, fetuses, one new-born child, and an adult in midsagittal section. The levels of the epiglottis and cricoid in all of these were taken off and used in this study. Merkel believes that even though the trachea extends lower in the new-born than in the embryo, the relative increase in tracheal length is more apparent than real and that this is due to slackening in growth of the vertebrae in late fetal life.

Symington (1885)[10] states that, in the new-born, the larynx and trachea terminate at a higher level than in the adult, but he was unable to find any definite statement as to their precise position in relation to the vertebral column. He found the larynx terminating opposite the middle of the fourth cervical vertebra and the trachea at the level of the lower border of the second thoracic vertebra; and he records the levels of the upper and lower limits of the larynx and of the bifurcation of the trachea in fetuses of 4, 6 and 7 months.

Scammon,[11] in his collection, has drawings of midsagittal sections of fetuses of the following crown-rump measurements: 34.7 mm., 43.3 mm. and 26.8 mm. These measurements, as all other measurements given in the literature as crown-rump alone, were converted to crown-heel measurements by the use of the formula which I [12] devised in 1921. The data from these three fetuses are used in this study.

Ballantyne (1891)[13] records the vertebral levels of the larynx of two 7 months, one 8 months and two 9 months fetuses, as well as of one new-orn child, and an adult in midsagiital section. The levels of the neck in the new-born than in the adult. He says, "In all proba-

8. Jackson: Footnote 3, second reference; Footnote 4, second reference.
9. Merkel: Footnote 2, fifth reference.
10. Symington: Footnote 2, seventh reference; Footnote 4, third reference.
11. Scammon: Footnote 2, sixth reference.
12. Noback, G. J.: Simple Methods of Correlating Crown-Rump and Crown-Heel Lengths of the Human Fetus, Anat. Rec. **23**:241, 1921.
13. Ballantyne: Footnote 2, first reference.

bility, in the case of the new-born infant with head erect, the larynx normally extends from a point opposite to the cartilage between the body and odontoid process of the axis to the level of the upper border of the fifth cervical vertebra, or to that of the disc between it and the fourth cervical vertebra. The descent of the larynx would seem, from Symington's measurements, to be a gradual process going on throughout childhood." The trachea, according to Ballantyne, lies at a higher level in the body of the infant than in the adult. He gives its limits as extending from the body of the fifth cervical to the body of the third thoracic vertebra. Birkenbusch (1890)[14] records the vertebral levels of the larynx in the case of two new-born infants.

Ribemont (1878)[15] illustrates a midsagittal section of a stillborn child in which the tip of the epiglottis is at the level of the lower border of the atlas and the inferior margin of the cricoid at the level of the middle of the fourth cervical vertebra.

Rudinger (1873)[16] pictures a midsagittal section of a new-born child in which the laryngeal levels are discernible.

The vertebral levels of the larynx and of the trachea in infancy and childhood have not been considered by many investigators. Symington (1887)[17] records these levels in infants 3½, 4, 6, 8 and 12 months, and in children 1 year and 10 months, 2 years and 2 months, 5 years, 6 years and in one child of 12 years. In another contribution, Symington (1881)[18] illustrates a midsagittal section of a 2 year old child in which he finds that the inferior margin of the cricoid cartilage is opposite the lower border of the fourth cervical vertebra and that the tracheal bifurcation is opposite the first thoracic vertebra. Symington concludes that the cervical part of the spinal column increases in length at a rate similar to the increases in length of the larynx, and that consequently the high position of the larynx in the neck of the child, as compared with the adult, cannot be due to its relatively small size. Symington's data are recorded in Chart 4.

Mettenheimer (1893)[19] records the levels of the inferior margin of the larynx and tracheal bifurcation in three new-born infants, and Chievitz (1899)[20] the levels of the epiglottis and larynx in two new-born children.

Birkenbusch (1890)[14] lists the vertebral levels of larynx and tracheal bifurcation in three children, 1, 6 and 13 years old, respectively.

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14. Birkenbusch: Footnote 3, first reference.
15. Ribemont: Footnote 3, sixth reference.
16. Rudinger: Footnote 3, seventh reference.
17. Symington: Footnote 4, third reference.
18. Symington: Footnote 2, seventh reference.
19. Mettenheimer: Footnote 3, fourth reference.
20. Chievitz: Footnote 2, second reference.

Sluka (1909),[21] after pouring Wood's metal into the trachea, determined the vertebral level of the bifurcation of the trachea by means of the roentgen ray. He concluded that the level of the tracheal bifurcation, without exception, in children between 1 and 4 years, was at the fourth thoracic vertebra; i. e., at the same level as in the adult.

Piersol (1908)[22] has an illustration which shows the tracheal bifurcation in a 2-year-old child as at the level of the fifth thoracic vertebra.

Dwight (1881)[23] says, "the bifurcation of the trachea is seen opposite the lower border of the fourth dorsal vertebra. This is practically its adult position in regard to the spine." The child described was 3 years old.

Zuckerkandl (1904)[24] illustrates a midsagittal section of a 7-year-old child in which the inferior margin of the larynx is opposite the sixth cervical vertebrae and the tracheal bifurcation between the fourth and fifth thoracic vertebrae.

The most extensive work on the level of the tracheal bifurcation in infancy and childhood is that of Engel (1913)[25] who made a roentgen-ray study of 112 living children between 2 and 8 years of age. He found that, after the second year, the levels, though fluctuating, remain practically uniform.

Keibel and Mall (1910)[26] state that the larynx is much higher in the embryo and in the fetus than in the adult, and that at the time of birth the descent of the larynx is not yet completed.

Gedgowd (1900)[27] concluded that the growth of the larynx and trachea, in childhood, corresponds more to the growth of the trunk and neck than to that of the body.

The vertebral levels of the lungs of fetus and infant are barely mentioned in the literature, practically the only reference to these levels being found in an article by Jackson (1909),[28] who says, "The lungs of the 11 millimeter embryo correspond approximately to the position later of the lung apex, lying opposite the last cervical and the first two thoracic segments . . . The migration continues downward along the vertebral column, however, so that the lung in the 17 millimeter embryo lies opposite the 4th-9th thoracic vertebrae. In the 31 millimeter embryo it is opposite the 1st-10th thoracic vertebrae and in the 65 millimeter it lies opposite the 2nd-11th thoracic vertebrae." Jackson's lengths are crown-rump, and have been converted into crown-heel, for use in this study, by my method.[12]

21. Sluka: Footnote 5, third reference.
22. Piersol: Footnote 3, fifth reference.
23. Dwight: Footnote 5, first reference.
24. Zuckerkandl: Footnote 5, fourth reference.
25. Engel: Footnote 4, first reference.
26. Keibel and Mall: Footnote 2, third reference.
27. Gedgowd: Footnote 5, second reference.
28. Jackson. Footnote 3, second reference.

Jackson,[29] in his personal collection, has drawings of a posterior dissection of 5 day old child, made by J. A. Watkins. These show the levels of the right lung to be between the middle of the first and the middle of the tenth thoracic vertebrae, and the levels of the left lung to be between the middle of the first thoracic and the upper border of the eleventh thoracic vertebrae.

All the data mentioned in the foregoing, with the addition of two of my specimens from children, aged 5 and 8 years, respectively, are recorded in Chart 4. Included in this illustration for the purpose of comparison are the vertebral levels of the larynx and trachea of the adult as given in texts and atlases.[6]

The observations on the levels of the larynx are more numerous, owing to the number of levels that have been obtained from the illustrations of midsagittal sections. There is a range of variation in these data because different observers studied individuals whose heads were in various postures; in some cases, the head was extended; in others, it was depressed, with a consequent influence on the levels of the larynx. In my series of cases, the head was always held in the same position; i. e., so that the inferior margin of the lower jaw was at a right angle to the long axis of the body. Taken as a whole, the levels of the larynx and trachea, except for this wide variation, coincide quite closely with the results obtained by me. This may be seen on comparing Charts 3 and 4.

The material in the literature for the period of infancy is rather meager, but, as is seen in Chart 4, these data indicate that the levels of the larynx and trachea are practically the same as those in late fetal life. This continuation of similar relationship of a group of organs to the body as a whole in both fetal life and early infancy is in agreement with the conclusions of Scammon (1922),[30] who has projected the fetal weight growth curves of many organs for several months after birth, and finds that the relative increase in weight in fetal life continues through approximately the first nine months of postnatal life.

The data for childhood are also quite meager, as is indicated by their number in Figure 4. However, in spite of the small number of cases, it is evident that, during later childhood, there is a distinct descent of the levels of the larynx and also a drop in the level of the tracheal bifurcation, which begins earlier than that of the larynx.

The data for the levels of the epiglottis, inferior border of the cricoid cartilage and of the bifurcation of the trachea are also plotted in Figure 4. In the case of the adult, we find, as in earlier life, that there are few definite data. The observations recorded in the plot are from

29. Jackson: Footnote 4, second reference.

30. Scammon, R. E.: On the Time and Mode of Transition from the Fetal to the Postnatal Phase of Growth in Man, Anat. Rec. **22**:34, 1922.

statements and illustrations in the literature. Each level observed ranges over the distance represented by three vertebrae and two disks.

OBSERVATIONS AND CONCLUSIONS

(*a*) *Topography of larynx, trachea and lungs during fetal life, infancy, childhood and adult life.*—The relation of the respiratory system to the vertebral column and the shifting of this system in a craniocaudal direction was studied by locating the levels of the following points: the tip of the epiglottis, the inferior margin of the cricoid cartilage, the tracheal bifurcation, the upper and lower limits of the lungs and the relation of the apex of each lung to the suprasternal notch. These levels were determined from my material on prenatal

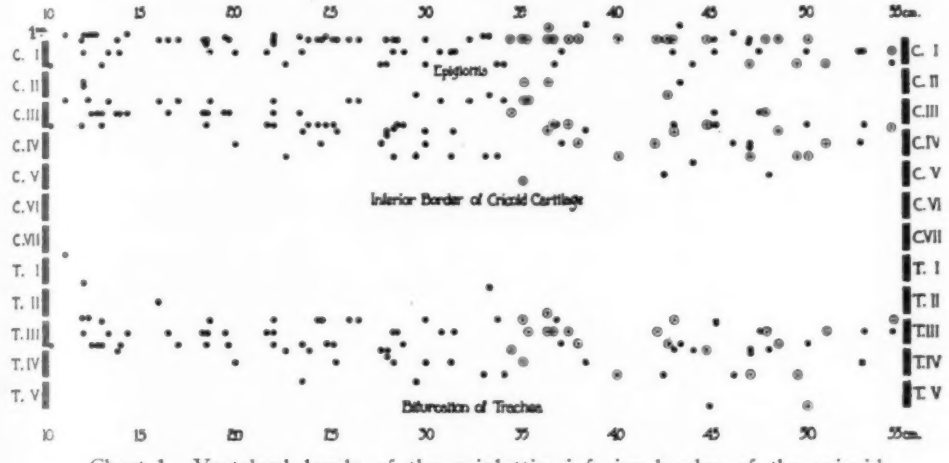

Chart 1.—Vertebral levels of the epiglottis, inferior border of the cricoid cartilage and the bifurcation of the trachea during fetal life and in the period of early infancy.

life, the new-born and two cases in children of 5 and 8 years, respectively. The literature was then examined and all available data regarding the levels of these points in the respiratory system were obtained as were also the data for infants, children and the adult.

The data obtained from my material was plotted on graph paper and are reproduced in Charts 1 to 7, inclusive.

Chart 1 presents the vertebral levels of the tip of the epiglottis, inferior margin of the cricoid cartilage and the tracheal bifurcation during prenatal life and in the new-born as determined by me. The level of the epiglottis in relation to the vertebral column has a slight variation but is limited to a span of a few millimeters superior to or inferior to the first cervical vertebra. The range of the level of the tip of the epiglottis is therefore limited to a distance which may be

regarded as equivalent to not more than one vertebra and intervertebral disk.

The descent of the epiglottis throughout the course of life from early prenatal to adult life is apparently as follows: The level is practically constant during prenatal life and infancy (Charts 1 and 4); a drop of two vertebrae and disks occurs between the first and thirteenth years, and a very slight descent occurs after this time, the level in the adult being quite constant.

The level of the inferior margin of the cricoid cartilage, and therefore of the inferior limit of the larynx, is less constant during fetal life

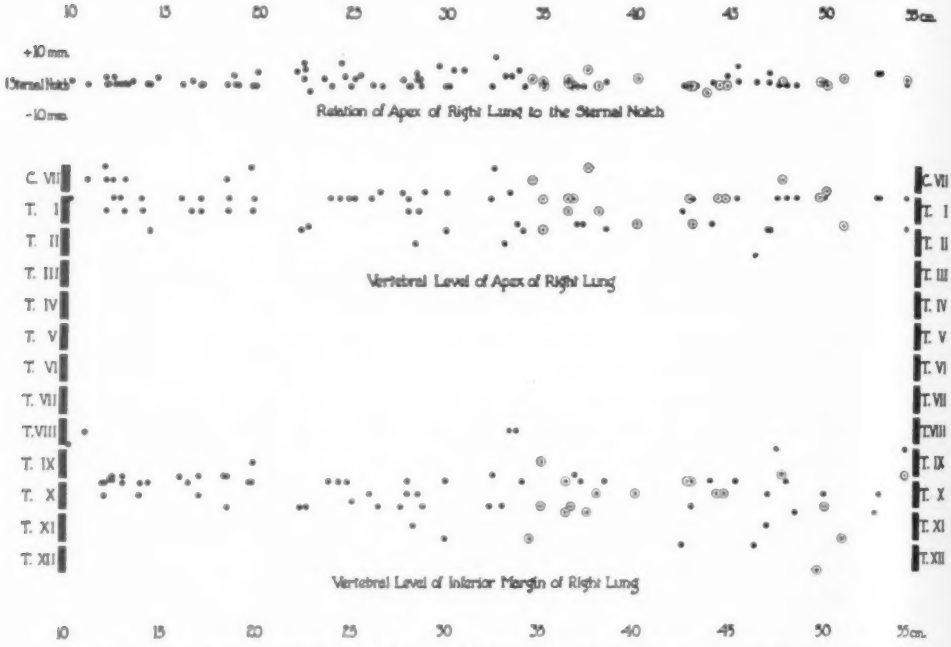

Chart 2.—The relation of the apex of the right lung to the suprasternal notch in the fetus and the new-born; the vertebral levels of the apex and of the inferior margin of the right lung.

and early infancy than is that of the epiglottis. In the 10 to 15 cm. group, it is located in the vicinity of the third cervical vertebrae; whereas, in the 45 to 50 cm. group, it has dropped to the vicinity of the fourth cervical vertebra. The descent is marked at all body lengths by wide variations, but as a whole it is a rather gradual one. The total drop between early fetal life and in early infancy is about equivalent to one vertebra and disk.

The descent of the inferior margin of the larynx considered from early fetal through adult life begins in the fourth fetal month and continues until birth (Chart 1), a drop of about one vertebra and one disk.

This level is maintained during infancy, but another descent occurs during childhood (Chart 4), so that by the thirteenth year the inferior margin of the cricoid cartilage has descended about two vertebra and one disk, opposite to the vicinity of the sixth cervical vertebra. The adult data indicates that there is a further descent of one vertebra and disk, to the seventh thoracic vertebral level.

The level of the tracheal bifurcation in the fetus and during the period of the new-born is also less constant than the level of the epiglottis. In the 10-15 cm. group, the average level is at the third thoracic vertebra, and in the 45-50 cm. group, around the third

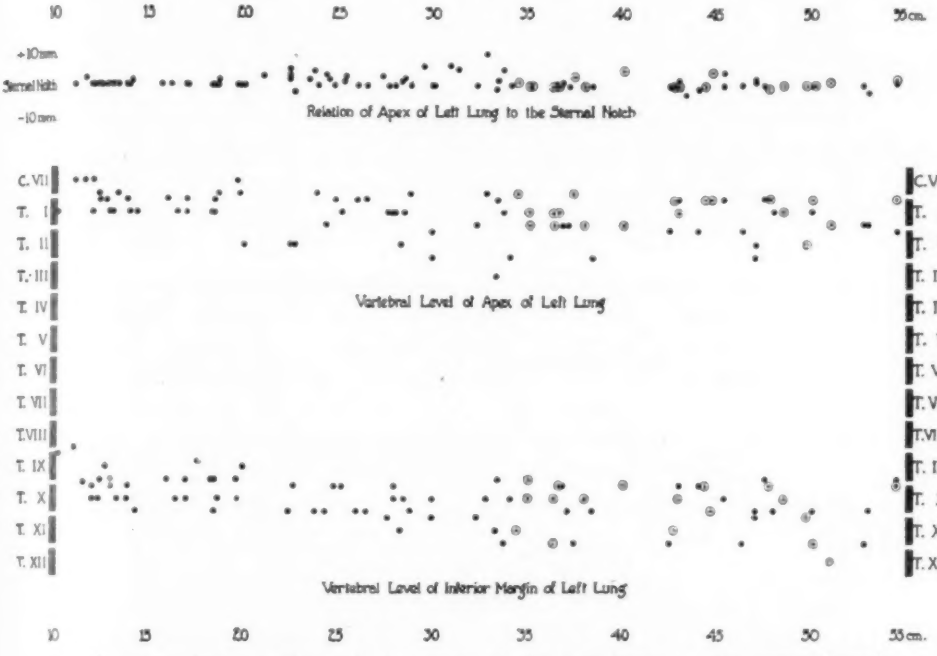

Chart 3.—The relation of the apex of the left lung to the suprasternal notch in the fetus and in the new-born; the vertebral levels of the apex and of the inferior margin of the left lung.

and fourth thoracic vertebrae. There is, therefore, an appreciable descent in prenatal life of an extent of one vertebra and one intervertebral disk. The descent, as in the case of the lower margin of the larynx, is gradual from early fetal life to the end of the prenatal period.

The bifurcation of the trachea considered from early fetal life through infancy, childhood and adult life (Charts 1 and 4) is as follows: Like the lower limit of the larynx, it begins a descent in the fourth fetal month from the level of the third thoracic vertebra to a region between the third and fourth thoracic vertebrae at birth. This level persists during the period of infancy, but early in childhood, at

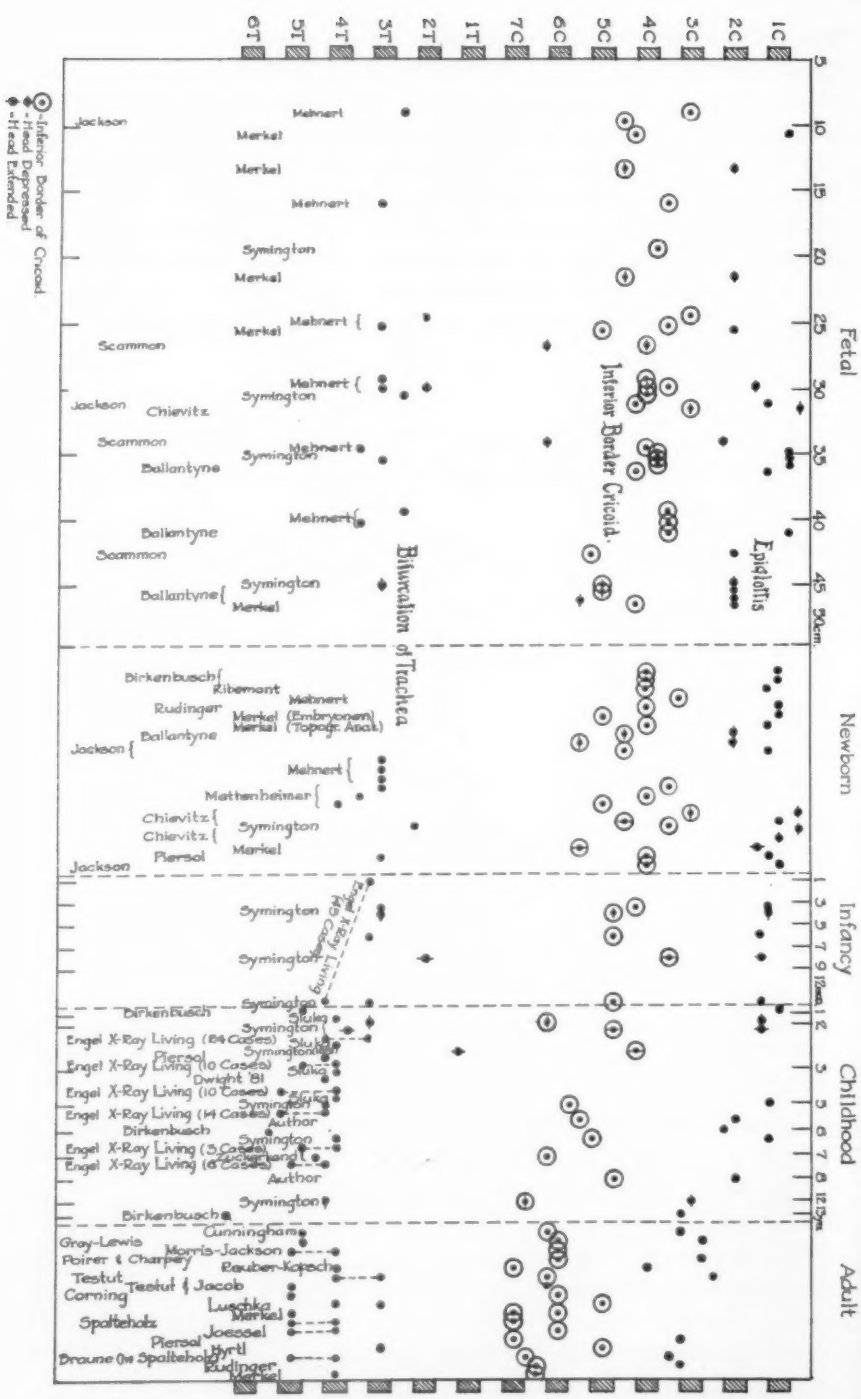

Chart 4.—The vertebral levels of the epiglottis, inferior margin of the cricoid cartilage and the tracheal bifurcation for prenatal and postnatal life as recorded in the literature.

about 2 years, another descent is apparent; and by the thirteenth year, the bifurcation has dropped a distance of one vertebra and disk to the level of the fourth and fifth thoracic vertebrae. This limit is apparently maintained during adult life.

Cameron (1922),[31] in a study of the abdominal viscera in fetal life, concludes that, of these organs, only the cecum, splenic flexure and sigmoid flexure undergo a descent in regard to the vertebral column, and Solhaug (1923)[32] finds that the bladder, uterus and ovaries of the pelvic organs descend caudalward.

In order to determine the descent of the lungs from early fetal life to the period of the new-born and in postnatal life, the uppermost and lowermost extent of these organs were noted in relation to the vertebral column and the data in the literature were surveyed. The relation of the upper poles of the lungs to the suprasternal notch was also noted. The data for the right lung are plotted in Chart 2.

The relation of the upper limit of the right lung to the sternal notch is a practically constant one during fetal life. It is found in the majority of cases to be at the same level as the notch, though there are some which extend above it, the greatest distance in these being 9 mm.

On plotting the upper limit of the right lung against the vertebral column, there seems to be a slight caudal shifting. The range is from the upper border of the seventh cervical to the inferior border of the second thoracic vertebra. The upper limit of the right lung makes a descent after the 20 cm. crown-heel length from between the seventh cervical and the first thoracic to between the first and second thoracic vertebra in the new-born, a descent of about one vertebra and disk.

The lower limit of the right lung in relation to the vertebral column shows a definite descent. In the 10-15 cm. group, the range is between the upper border of the ninth and the lower border of the tenth thoracic vertebra. From the 25 cm. length to the end of the series, the drop is distinct, as is indicated by the fact that the inferior margin of the lungs descends as low as the inferior margin of the twelfth thoracic vertebra in the full-term new-born child. The descent approximates a distance measured by one vertebra and intervertebral disk.

The relation of the left lung to the sternal notch and to the vertebral column is shown in Chart 3. The relation to the sternal notch is quite similar to that of the right lung. The majority are level with the notch though there are a number which extend several millimeters above and a few that are very slightly below it.

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31. Cameron, A. L.: The Topography of the Abdominal Viscera in the Late Embryonic and the Fetal Period of Man as Determined by Graphic Reconstruction, abstr., Anat. Rec. **23**:12, 1922.

32. Solhaug, S. B.: A Study of the Developmental Topography of the Pelvic Organs of the Female Fetus, Thesis, Doctor of Philosophy, University of Minnesota, 1923.

The upper limit of the left lung (Chart 3) undergoes slight descent after the 20 cm. body length. Up to this length, the range is from the upper margin of the seventh cervical to the lower margin of the first thoracic vertebra. The drop from this point on to the condition as found in the new-born infant is of about one vertebra and disk, and the range extends from the upper margin of the first to the middle of the second thoracic vertebra at birth. The descent is slight, as was the case in the right lung, and it is probable that this descent is real, though

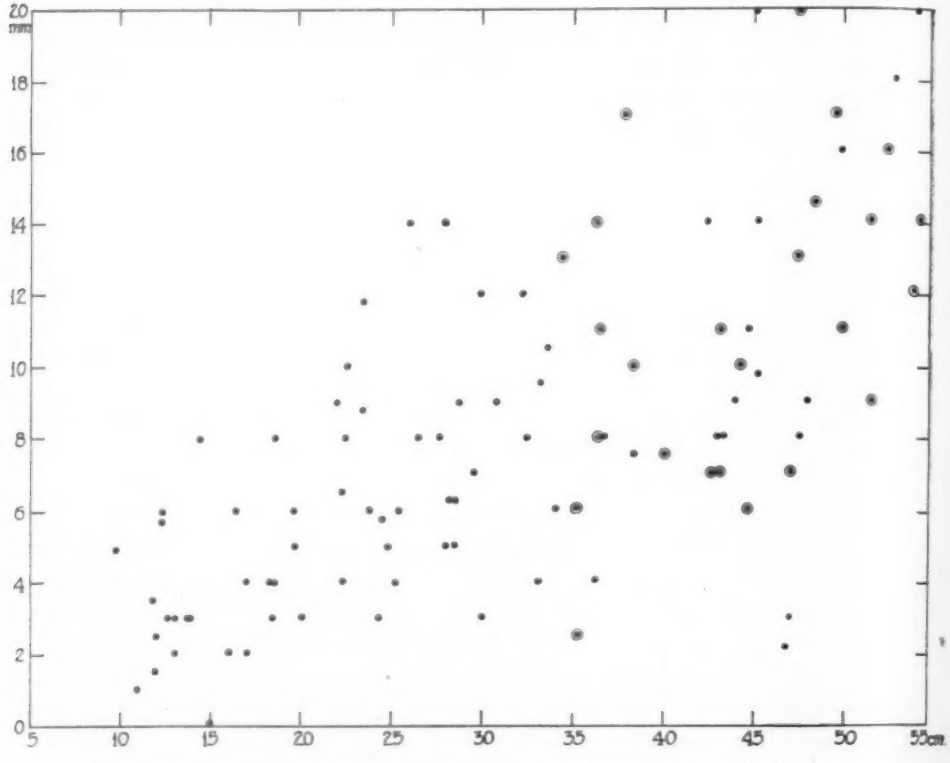

Chart 5.—Field graph of the depth of the cardiac notch plotted against total body length in the fetus and the new-born.

it must be slight and does not occur until after the fetus has attained a length of about 20 cm. total body length, or beginning in the fifth fetal month.

The inferior margin of the left lung (Chart 3), like that of the right lung, undergoes a definite descent. Up to a total body length of 20 cm., the range is from the upper margin of the ninth to the inferior margin of the tenth thoracic vertebra. From this point on, the descent is clearly indicated, and in the new-born group, the range has dropped

to the levels between the middle of the tenth and the middle of the eleventh thoracic vertebra, a total drop of one vertebra and disk.

Considering both lungs, it may be concluded that the relation to the sternal notch is constant; that the upper limit of the lungs may descend slightly, and that the lower limit of the lungs, until the period of early infancy, undergoes a more definite descent of from one to two vertebrae in extent.

The vertebral levels of the adult (Chart 4) as given in the literature range as follows: The upper limit at the first thoracic vertebra and the lower limit opposite the ninth to the twelfth thoracic vertebrae. The adult vertebral levels of the lungs correspond quite closely to those found in the new-born infant. Therefore, any increase in length of

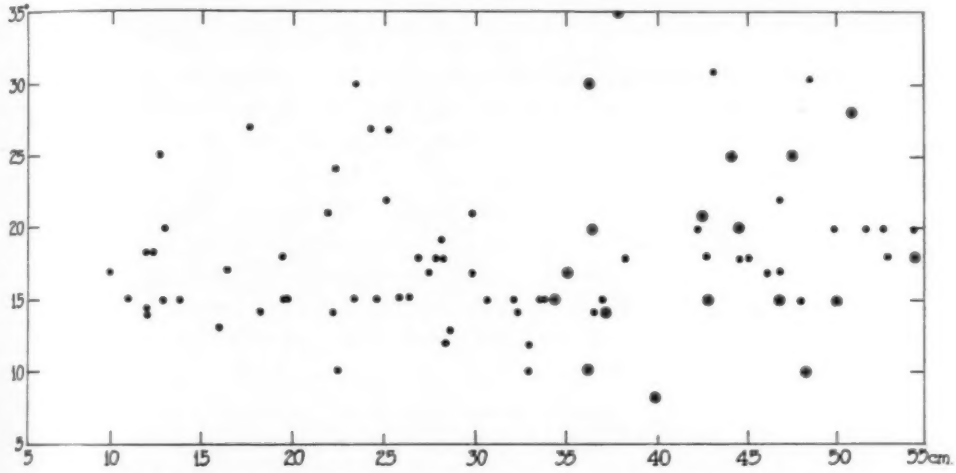

Chart 6.—Field graph of the angle of the right bronchus plotted against total body length in the fetus and the new-born.

the lungs in postnatal life must be accompanied by a corresponding increase in length of thorax.

(*b*) *The lobation of the lungs.*—Many observers have noted the variation in lobation of the lungs, notably Henle [33] who not only described them but diagrammed several of them. More recently, Spandolini,[34] in a comprehensive study of the morphology of the lungs, utilizing a series of 175 individuals, 125 adults and fifty fetuses of various stages of development, discusses lobation of the lungs.

My material consists of the lungs of a series of 101 fetuses and new-born children. It was found that the greater amount of variation

33. Henle, J.: Handbuch der systematischen Anatomie des Menschen, Braunschweig, 1873, Ed. 2, Vol. 2, p. 274 and Figure 207.

34. Spandolini, I.: Contributo allo studio della morphologia del pulmone, Arch. ital. di Anat. e di Embryol. **2**:604, 1913.

occurs in the right lung, since thirty-seven, or 36.8 per cent., of the total 101 right lungs were typical in their lobation; whereas, sixty-four, or 63.3 per cent., were atypical. Variation from the normal lobation in the left lung is rather infrequent, as is indicated by the fact that but 5.8 per cent., or six out of the total of 101, were abnormal in their lobation, and ninety-five, or 94.2 per cent., were typical.

The variation from the accepted normal of three lobes in the right lung and two lobes in the left lung may take form in either an increase in the number of fissures or a decrease due to their underdevelopment.

In the right lung, it was found that incomplete development of the fissures was the more frequent, with a total of sixty-one, or 60.3 per cent., of the cases showing this deficiency, and but three cases, or 2.9 per cent., presenting accessory or supernumerary fissures. The incompleteness of fissures varies greatly in extent, there being several

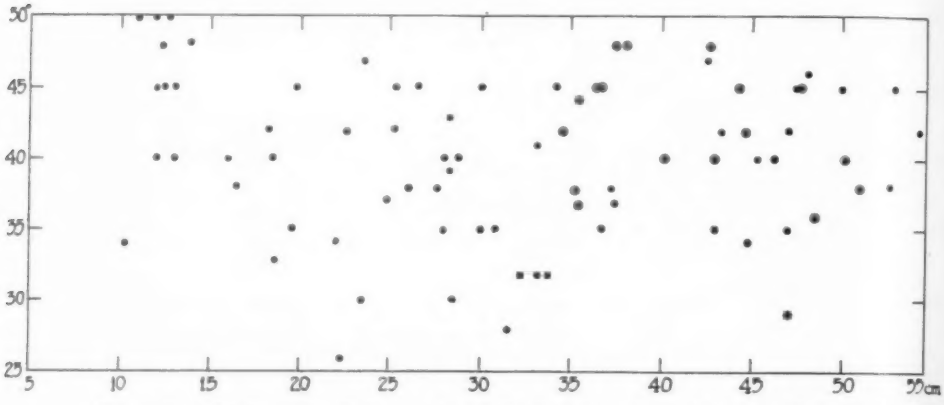

Chart 7.—Field graph of the angle of the left bronchus plotted against total body length in the fetus and the new-born.

cases of special note. One right lung had a total absence of the horizontal fissure, and the oblique fissure did not reach the base of the lung. Another modification of the fissuration of especial interest is one which was present in four of the right lungs. Here it was found that the horizontal fissure was not complete in that it failed to reach the median border of the lung, and that the oblique fissure, instead of being quite straight in its course, had, at the level of the incomplete horizontal fissure, a pyramidal tonguelike process which projected medially and inferiorly into the underdeveloped horizontal fissure. The presence of supernumerary fissures in the right lung is not frequent, there being but three cases, or 2.9 per cent., of the total number. Of these three cases there were two in which the extra fissure extended laterally from the oblique fissure at the level of the horizontal fissure to such an extent that one might say that these lungs were composed of four lobes.

In the left lung, abnormal fissuration is relatively infrequent, there being but six of the total of 101 left lungs with abnormal lobation. Of these, three, or 2.9 per cent., of the total had incomplete fissures, and three, or 2.9 per cent., were lungs in which there were supernumerary fissures. The latter were incomplete horizontal fissures which tended to divide the lung into three lobes similar to those normally found in the right lung.

Spandolini,[34] in his series of fifty fetuses and new-born children, found that only 49.1 per cent. of the right lungs were normal in the oblique fissure and but 36.7 per cent. of the horizontal fissures were complete. He found that the fissures in the left lung were normal in but 66 per cent. of the cases. His findings in the left lung are much higher than those in my series, in which the normally fissured lungs totaled 95, or 94.2 per cent.

(*c*) *The angles of divergence of the bronchi.*—The deviation of the right bronchus from the midsagittal plane (Chart 6) shows great variation in all of the groups of specimens. In the 10 to 15 cm. group, it ranges from 13.2 to 35.8 degrees, and in the new-born group, from 10 to 30 degrees. However, throughout fetal life, the greater number of cases are grouped between 14 and 22 degrees and the average may be taken as about 18 degrees.

The deviation of the left bronchus from the midsagittal plane, like that of the right bronchus, varies to a great extent, and the angle is much greater than is that of the right bronchus. The range (Chart 7) in the 10 to 15 cm. group is from 34 to 50 degrees and in the new-born infants from 38 to 45 degrees. The average angle for the left bronchus may be stated to be about 42 degrees.

(*d*) *The cardiac notch.*—The cardiac notch (Chart 5) shows a tendency to increase in size along with the increase in total body length, there being, however, very wide fluctuations in this measurement throughout the fetal period. The measurement in the 10 to 15 cm. group is from 1.0 to 6.0 mm., and, in the new-born group, ranges from 2.0 to 20.0 mm.

SUMMARY

1. The descent of the respiratory system in relation to the vertebral column during childhood is not peculiar to this period in the development of the individual. It is merely a stage in a process which is already manifested in early fetal life and which continues to operate through infancy, childhood and maturity.

2. The larynx. During fetal life, the topography of the epiglottis shows practically no change. It remains quite constantly opposite the first cervical vertebra. This level persists through infancy and child-

hood until puberty, when the adult relationship is attained, i. e., it lies opposite the third cervical vertebra.

The inferior margin of the cricoid cartilage, and therefore the lower limit of the larynx, descends during the course of prenatal life from opposite the third to opposite the fourth cervical vertebra, a distance represented by one vertebra and intervertebral disk. During infancy, this relationship remains constant; but during later childhood, another descent to the level of the sixth cervical vertebra takes place, a drop of two vertebrae and one disk. With the attainment of maturity, a further descent of one vertebrae and disk has occurred, so that the inferior limit of the larynx is then opposite the seventh cervical vertebra.

3. The bifurcation of the trachea. The tracheal bifurcation undergoes a descent caudalward in relation to the vertebral column during fetal life. It drops from opposite the third to opposite the fourth thoracic vertebra, a descent of one vertebra and disk. The natal relationship persists during infancy, but in childhood another descent takes place, and by puberty the bifurcation is opposite an area between the fourth and fifth thoracic vertebrae. This level is then maintained, apparently, through adult life.

4. Topography of the lungs. The apices of the lungs remain at practically the same level as the suprasternal notch throughout the course of fetal life.

The upper poles of the lungs in relation to the vertebral column undergo a slight descent during prenatal life from a level opposite the seventh cervical or first thoracic vertebra to the upper margin of the second thoracic vertebra, a distance of one vertebra or less. This level is apparently maintained throughout the course of postnatal life.

The inferior margins of the lungs during fetal life undergo a descent from between the ninth and tenth to opposite the tenth to twelfth thoracic vertebrae, a distance equivalent to slightly more than one vertebra and disk. The latter level, present at birth, coincides quite closely to the levels as given in the standard texts and atlases for the adult, thus indicating the probability that the postnatal growth in length of the lungs is closely correlated with the increase in length of the thorax.

5. The lobes of the left lung in the human fetus do not vary much from the condition in the adult, there being but 5.8 per cent. of the total with atypical lobation. The lobes of the right lung depart quite markedly from the conditions usually described in the adult, there being but 36.8 per cent. of the total with the typical three-lobed condition.

6. The depth of the cardiac notch. The extent of the cardiac notch during prenatal life is extremely variable in a group of cases of the same body length. There is, however, a general increase in depth with increase in total body length.

THE EFFECT OF INADEQUATE DIET ON THE INORGANIC SALT CONTENT OF MOTHER'S MILK*

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It is well recognized that the milk of the dairy animal has a marked tendency to remain constant in composition even under adverse conditions, changes in the diet, particularly in respect to the inorganic constituents, not readily affecting the concentration of the various components.

In a review of the subject of milk secretion as related to diet, E. B. Meigs [1] has given an exposition of the dietary factors influential in increasing or diminishing both the milk yield and the concentration of its various constituents, as brought out by the extensive experimental work which has been carried on with dairy and other animals. In brief, it has been found that in early lactation the cow has a remarkable power to secrete milk normal in yield and composition on inadequate rations, the shortage being supplied at the expense of its own body, as shown by loss of weight. In later stages of lactation, the total milk yield and frequently the concentration of protein and of fat can be considerably affected in a short time by changes in the organic components of the diet, most readily by decrease or increase in the amount of protein or of total nutrients in the rations. On the other hand, it may take weeks or months before the effect of the reduction of inorganic constituents in the diet can be seen in the milk.

Most of the experimental work with animals on changes in inorganic salt content of the diet in relation to milk composition have been concerned with sodium chlorid, calcium salts and phosphates. Many experiments with sodium chlorid have shown that neither additions of that salt to the diet in considerable amounts nor reductions in the intake, even to total deprivation, have any significant effect on its concentration in the milk.

Denis and Sisson [2] have made some interesting experiments concerning inorganic salt in milking goats. They found no change in the chlorin content of the milk of one animal after twenty-four days on

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1. Meigs, E. B.: Physiol. Rev. **2**:204 (April) 1922.

2. Denis, W., and Sisson, W. R.: J. Biol. Chem. **46**:483 (May) 1921.

a diet without sodium chlorid, and no increase after feeding the same animal relatively high doses of that salt for eleven days. Only when doses were given large enough to raise the chlorin content of the blood plasma 18 per cent. was there an increase in the chlorin concentration of the milk, and with this occurred a greatly diminished milk yield. Later,[3] they tried to increase the calcium concentration in the milk of goats by feeding large doses of calcium chlorid, but obtained negative results. The chlorin content of both blood and milk was increased in two of the animals, and in the blood only in a third. Intravenous injection of 1.87 gm. of calcium chlorid in a volume of 75 c.c. resulted in a large increase in both calcium and chlorin content of the blood and in the chlorin concentration of the milk, but there was no increase of the calcium of the milk, which was tested at intervals during the day.

Jordan, Hart and Patten[4] have shown that a reduction of phosphorus in the rations of cattle reduces the percentage of fat in the milk without affecting the total yield or the phosphorus content of the milk, and increasing the phosphorus intake results in an increased proportion of fat in the milk, but no increase of the phosphorus.

Several groups of investigators, notably Forbes and his collaborators[5] and Hart and his associates,[6] have brought out the striking fact that the milking cow or goat can have a negative calcium and phosphorus balance from an insufficient supply of these elements in the diet or of the vitamins that promote their assimilation or of both factors, and yet show normal calcium and phosphorus content of both blood and milk and little immediate diminution in the milk supply. This is to be attributed to the ability of these animals to take large amounts of calcium and phosphorus from their bones to supply the lack in their rations. Incidentally, the tables presented by Hart and others show, in the case of one goat with a small and rapidly diminishing milk supply, an abnormally high concentration of calcium and phosphorus in the milk.

Meigs[1] reports the experiments of Fingerling[7] in which he reduced the calcium and phosphorus intake of lactating goats, with at first no effect on the milk, but with immediate loss of these elements from the animals' bodies. After several weeks, the milk yield fell off and its

3. Denis, W.; Sisson, W. R., and Aldrich, M.: J. Biol. Chem. **50**:315 (Feb.) 1922.

4. Jordan, W. H.; Hart, E. B., and Patten, A. J.: Am. J. Physiol. **16**:268, 1906.

5. Forbes, E. B., et al.: Bull. Ohio Agricultural Exper. Station, No. 295, 1916; No. 308, 1917; No. 330, 1918.

6. Hart, E. B.; McCollum, E. V., and Humphrey, G. C.: Am. J. Physiol. **24**:86, 1909. Hart, E. B.; Steenbock, H.; Hoppert, C. A., and Humphrey, G. C.: J. Biol. Chem. **53**:21 (July) 1922.

7. Fingerling, G.: Die landwirtsch. Vers.-Stat. **75**:1, 1911.

calcium and phosphorus concentration rose, though the total amount of both minerals excreted in the milk was decreased. Return of the normal amount of calcium and phosphorus to the rations restored the milk to normal.

Meigs and Woodward [8] found evidence sufficient for them to conclude that the calcium and phosphorus content of the diet of the period preceding lactation is more important in the effect on the milk secretion than that during lactation and that the full effect of deficiencies in these elements may not become apparent for years.

In the investigation of the effect of diet on the salt content, much less work has been done on human milk than on the milk of lower animals. Analyses of human milk recorded in the literature [9] show considerable variation in concentration of most of the inorganic constituents; but as these values are not correlated with definite information concerning the diets of the mothers, the variation proves nothing for the question under discussion. An average of ten samples of late milk (at ten months or later) show a lower calcium, magnesium and phosphorus content and higher concentration of sodium and chlorin than the corresponding averages for mature milk (that secreted from the beginning of the second month to the tenth month), and these changes are regularly associated with a considerably reduced milk production. A table including these supposedly normal values will be presented later.

Bahrdt and Edelstein [10] found a lowered content of calcium in the milk of mothers of rachitic and anemic children, but they consider the number of their analyses too few to give much weight to the observation. They gave calcium to a mother but obtained no definite effect on the content of calcium in the milk. Bunge, as quoted by Freund,[11] found no significant effect on the chlorin content of the milk from giving a nursing mother a diet free from sodium chlorid, and later one containing 30 gm. of the salt in the day's food. Sisson and Denis,[12] who have recently made a study of the chlorin content of human milk, found wide variations in both directions in samples of milk from different individuals and in those from the same individual collected at different times. They conclude, however, that the milk of the normal mother giving regularly a normal supply, after the second week of

8. Meigs, E. B., and Woodward, T. E.: Bull. U. S. Dept. Agriculture, No. 945, 1921.

9. Talbot, F. B.: A Summary of Present Knowledge of Human Milk, Am. J. Dis. Child. **7**:445 (June) 1914. Holt, L. E.; Courtney, A. M., and Fales, H. L.: A Chemical Study of Woman's Milk, Especially Its Inorganic Constituents, Am. J. Dis. Child. **10**:229 (Oct.) 1915.

10. Bahrdt, H., and Edelstein, H.: Jahrb. Kinderh. **72**:16, 1910.

11. Freund, W.: Jahrb. Kinderh. **48**:137, 1898.

12. Sisson, W. R., and Denis, W.: Observations on Salt Content of Human Milk, J. A. M. A. **75**:601 (Aug. 28) 1920. Sission, W. R., and Denis, W.: Studies on Inorganic Constituents of Milk, Am. J. Dis. Child. **21**:389 (April) 1921.

lactation to the end of the sixth month, is most constant in chlorin content. They found no effect produced by ingestion of sodium chlorid, but they did not use excessive doses.

Studies of the diets of mothers nursing rachitic infants, made by Hess and Unger,[13] and by Dunham, Willis and Guy, as quoted by E. A. Park [14] in his recent review of the subject of rickets, although no milk analyses are reported, suggest that, in at least some of the cases, the milk may have been abnormal in calcium or phosphorus content as well as in other respects. Hess and Unger found that the diets of these women were made up of meat, fish, rice, potatoes, cereal, tea and coffee, with little milk and what vegetables were included mostly canned. Dunham, Willis and Guy found that the majority of the diets which they investigated provided less than the caloric requirement of mother plus child and that they were almost entirely lacking in fresh fruit and vegetables. In certain cases, the diet was low in calcium content, and in some, in phosphorus. They found in some instances that the mother's milk was low in caloric value.

With human milk as with that of the lower animals, though the tendency may be to constancy in concentration of inorganic constituents, the probability is that changes may be brought about by long-continued deficient or ill-balanced diets.

Four more or less defective diets of nursing mothers have come under observation at the Hospital for Sick Children during the last fifteen months. The diets are reported as those used during the period of lactation. The details were necessarily obtained from the mothers themselves and some allowance must be made for individual judgment regarding quantities taken and for minor omissions. Making due allowance, however, for such errors, the defects in the diets are sufficiently evident.

The milk of each mother was obtained in quantity under conditions calculated to insure typical samples. The content of calcium, magnesium, total phosphorus, chlorin, sodium and potassium was determined according to standard gravimetric methods. Estimation was made also of the calcium and phosphorus content of the infants' serum. The caloric values of the protein, fat and carbohydrate components of the diets were calculated according to the estimates given in Locke's "Food Values." As reported, they represent, unless otherwise stated, approximately the daily intake. Hoobler,[15] in a study of the protein intake of nursing mothers, gives the caloric value and the proportion

13. Hess, A. F., and Unger, L. J.: Diet of Negro Mother, J. A. M. A. **70**:900 (March 30) 1918.

14. Park, E. A.: Physiol. Rev. **3**:106 (Jan.) 1923.

15. Hoobler, B. R.: Protein Diet and Human Milk, Am. J. Dis. Child. **14**:105 (Aug.) 1917.

of protein in a series of diets which he used. The total calories of the diets ranged from about 2,000 to 4,000, mostly from 2,300 to 3,000. He states that the diets including 3,700 calories resulted in overfeeding and did not give as good results as those of a value of 3,000. He emphasizes the importance of the nutritive ratio of the diet. By this is meant the ratio of the number of calories provided by protein to the sum of those provided by fat and by carbohydrate. This ratio for his series of diets varied between 1:4 and 1:15, but he considers the optimum range to be from 1:4 to 1:6. For cattle on standard rations, the values range from 1:4.5 to 1:8.5. This study of Hoobler's provides a useful standard of comparison.

OBSERVATIONS IN FOUR CASES

CASE 1.—The diet consisted of approximately 33 ounces (976 c.c.) of milk (taken partly in two cups of cocoa and one cup of tea and on the cereal), one egg, a small amount of cornmeal porridge, two slices of bread and butter, one serving of potato, one serving of carrots, cauliflower or peas several times during the week but not every day, two small servings of preserved fruit and two or three chocolates. Sugar was added only to the cocoa. No meat had been eaten for about two years, but meat gravy was sometimes taken.

The caloric value was 1,800; the nutritive ratio (approximate), 1:6.5. The chief defects were a too low nutritive value and lack of fruit and vegetables. The distribution of calories as fat, protein and carbohydrate in this diet is good and the quantity of milk, which provided a fair supply of minerals, might have been sufficient if the diet had been satisfactory in other respects.

The child, aged 7 months, weight 16 pounds (7,257 gm.), had been nursed from birth. She was admitted to the hospital because of having bad stools and convulsions. She showed slight craniotabes and had no teeth. The blood calcium content was 9.7 mg. per hundred cubic centimeters of serum. The blood phosphorus was not determined.

The milk secretion averaged 18 to 19 ounces (532 to 562 c.c.) a day. The analyses showed its concentration of calcium and magnesium to be lower than the normal average, of potassium and phosphorus, higher; while that of sodium and chlorin was nearly the normal. No values, however, were outside the extremes reported for supposedly normal milks.

CASE 2.—This diet included about 13 ounces (385 c.c.) of milk (taken wholly in eight cups of tea and on porridge and pudding), three and one-half slices of bread with oleomargarin, one serving of oatmeal or cornmeal porridge, one of potato, one of turnips or carrots about once a week, about 8 ounces (236 c.c.) of vegetable soup once a week, one serving of thoroughly stewed lean meat, one small piece of bacon once a week, one serving of rice pudding twice a week and one of stewed fruit about once a week. Sugar was taken in tea and on porridge and pudding in moderate amounts.

The caloric value was slightly over 2,000; the nutritive ratio (approximate), 1:6. The chief defects were too low nutritive value to supply the need of mother plus child, too great a proportion of carbohydrate and too little of fat, the small supply of sources of fat-soluble vitamin, lack of fruit and vegetables and far too little milk to provide the mineral requirement.

The child, aged 12 months, weight 21 pounds and 14 ounces (9,912 gm.), had been nursed from birth, receiving in addition during the preceding five months a little bread or bread and cow's milk. He was admitted to the hospital suffering from tetany, having spasms of the hands and feet. He was well-

nourished, but showed through roentgen-ray examination signs of acute rickets. The blood calcium content was 5.2 mg. per hundred cubic centimeters of serum, the phosphorus, 6.8.

The milk supply seemed to be abundant, though the child nursed irregularly. One day he took 39 ounces (1,153 c.c.). Analyses showed calcium and magnesium content less than the normal average for mature milk but only slightly less than that for late milk. The content of potassium and of phosphorus was higher than normal and that of sodium and of chlorin nearly normal. No values fell outside the extremes found in the case of normal milk.

CASE 3.—This mother was nursing twins. The diet included from 8 to 10 ounces (236 to 296 c.c.) of milk (taken wholly in two or three cups of tea and one of cocoa and on pudding), one egg, about four slices of white or brown bread with butter, one pork chop or one serving of minced meat, one potato, one serving of pudding, from three to five soda wafers or other biscuit and occasionally a piece of cake. She took sugar in the tea and cocoa, and on the pudding. Her intake included also eight cups of a galactagogue extract of cotton seed, which on analysis showed a high nitrogen content that, if computed entirely as protein, would make the substance 65 per cent. protein. It contained also 2.5 per cent. of fat or other ether extractives, 1.75 per cent. calcium, computed as calcium oxid, and 20 per cent. of reducing substances after hydrolysis. Before hydrolysis, there was no reduction. The iodin test showed no starch present. There was less sweet taste than would be expected if 20 per cent. cane sugar were present. Giving the benefit of the doubt as to both protein and sugar content, 300 calories have been alloted to the galactagogue added to the diet.

The total calories were 2,300; the nutritive ratio (aproximate), 1:3.5 (assuming the galactagogue to be 65 per cent. protein). The chief defects were: total caloric intake too low for mother and two infants, low proportion of fat in any case and too high proportion of protein, if the galactagogue contained the maximum amount of protein, entire lack of fruit and of vegetables other than potato and an entirely inadequate supply of milk. The low mineral content of the regular diet was increased to some extent by the calcium contained in the galactagogue.

The children, aged 4 months, weights 13 pounds and 1 ounce (5,925 gm.), 13 pounds and 12 ounces (6,237 gm.), had been nursed from birth. They were admitted to the hospital because of a cough and fever. Both had marked craniotabes and secondary anemia, and there was roentgen-ray evidence of chronic or healing rickets. The smaller child was given a blood transfusion after admission. This child's blood had a calcium content of 9.2 mg. per hundred cubic centimeters of serum and a phosphorus content of 2.6. The blood calcium of the other child was 9.7 mg. per hundred cubic centimeters and the phosphorus, 4.6 mg.

The milk production was about 20 ounces (591.5 c.c.) a day. It was found to be much lower in calcium and magnesium content than normal milk. The content of potassium and of phosphorus was nearly normal, that of sodium rather high and of chlorin rather low. The values found for calcium and magnesium fell below the extremes reported for normal mature milk.

CASE 4.—This diet was the most abnormal in the series. It consisted of one or two fried eggs, meat three times daily, usually beef, preferred fat, occasionally pork chops, about two slices of bread with no butter, two servings of potato and sauerkraut once a week.

The caloric value was 1,700; the nutritive ratio (approximate), 1:2.3. The chief defects were a too low nutritive value, too great proportion of protein and too little of carbohydrate, too much meat, entire lack of milk, butter, fruit and of vegetables other than potato and the weekly serving of sauerkraut. The supply of minerals and of vitamins must have been far below the requirement.

The child, aged 6 months, weight 13 pounds and 13 ounces (6,264 gm.), had been nursed from birth, but was receiving at the time four or five supplementary feedings a day of cow's milk. He was admitted to the hospital for treatment of a subcutaneous abscess. He showed marked evidences of rickets including those revealed by roentgen-ray examination. The calcium content of the blood serum was 9.2 mg. per hundred cubic centimeters; that of phosphorus, 2.8 mg.

The supply of milk was small and nursing was stopped entirely soon after his admission to the hospital. The milk analysis showed very low calcium and phosphorus concentration, rather low magnesium and normal potassium, and abnormally high sodium and chlorin concentrations. The value for calcium

TABLE 1.—*Salt Content of Milk and Calcium and Phosphorus of Infant's Blood*

	Milk Salts, Gm. per Hundred C.c.			
	Case 1	Case 2	Case 3	Case 4
Total salts	0.2343	0.2076	0.1823	0.1928
Calcium oxid	0.0363	0.0367	0.0290	0.0290
Magnesium oxid	0.0056	0.0067	0.0035	0.0074
Phosphorus pentoxid	0.0512	0.0541	0.0418	0.0258
Chlorin	0.0392	0.0379	0.0309	0.0475
Potassium oxid	0.0801	0.0723	0.0684	0.0618
Sodium oxid	0.0145	0.0161	0.0195	0.0284
	Contents Infant Serum, Mg. per Hundred C.c.			
Calcium	9.7	5.2	9.7-9.2 (Larger of twins)	9.2
Phosphorus	...	6.8	4.6-2.6 (Smaller of twins)	2.8

TABLE 2.—*Salt Content of Normal Milk*

	Milk Salts, Gm. per Hundred C.c.					
	Average for 17* Samples of Mature Milk	Extreme Values for 17 Samples of Mature Milk	Average for 10* Samples of Late Milk	Average for 11† Samples of Mature Milk	Extreme Values for 11 Samples of Mature Milk	Average for 3† Samples of Late Milk
Total salts	0.2063	0.1590-0.2433	0.1978	0.1955	0.1790-0.2484	0.1512
Calcium oxid	0.0472	0.0295-0.0702	0.0390	0.0416	0.0328-0.0567	0.0290
Magnesium oxid	0.0081	0.0052-0.0106	0.0070	0.0082	0.0060-0.0116	0.0069
Phosphorus pentoxid	0.0345	0.0212-0.0514	0.0304	0.0409	0.0260-0.0585	0.0385
Chlorin	0.0355	0.0251-0.0444	0.0442	0.0340	0.0244-0.0468	0.0245
Potassium oxid	0.0574	0.0366-0.0714	0.0575	0.0632	0.0522-0.0848	0.0451
Sodium oxid	0.0153	0.0031-0.0250	0.0195	0.0189	0.0049-0.0258	0.0165

* From twenty-seven analyses of Holt, Courtney and Fales.
† Analyses of Abderhalden, Blauberg, Pelka, Soldner and E. Schloss.

was lower than the extreme for normal milk, that for phosphorus barely within the limits; while those for sodium and chlorin were greater than the normal extremes.

Table 1 gives the values found for the various salts in the four samples of milk and also the calcium and phosphorus content of the blood serum of the infants. Table 2 gives the averages and the extreme values found for the inorganic constituents of normal milk, which have been used above for comparison.

It is significant that the two specimens of milk in which the irregularities in salt content were greater than those presenting the

extreme values for corresponding salts of normal milk were those of the two mothers whose diets showed the most glaring defects. Milk was entirely lacking or provided in an almost negligible amount, and fruit was entirely lacking, as was practicably every vegetable but potato. In addition, the total supply of nutriment was undoubtedly below the requirement. One of the twins in the one case, as well as the child of the other mother just referred to, had an abnormally low phosphorus content of the blood serum, the typical rachitic finding.

Continued use of a deficient diet by the nursing mother may have serious effects on the child, especially in the later stages of lactation, when the mother's reserve has become depleted. Observations on the lower animals even suggest that, if the diet of the mother has been habitually below her own need in one or more constituents, her milk may be below standard even from the beginning of lactation.[16]

The determination of calcium and phosphorus in the serum in the two additional cases here described was made by Dr. Tisdall.

16. Two of the cases described have already been reported (Brown, Alan; Courtney, A. M.; Tisdall, F. F., and MacLachlan, I. F.: A Critical Study of Two Cases of Rickets Developing in Breast Fed Infants, Arch. Pediat. **39**:559 (Sept.) 1922.

THE ACIDITY OF THE GASTRIC CONTENTS OF INFANTS*

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The object of this paper is to consider the acidity of the gastric contents of infants under normal and pathologic conditions; the influence of the diet on the degree of acidity, and the practical significance of the gastric acidity in relation to infant feeding.

There are various means of determining the degree of gastric acidity and of expressing the results. The titration of the gastric contents, following a test meal, has been the method most used in the case of adults, and the results are usually expressed in terms of "total hydrochloric acid," "free hydrochloric acid" and "combined hydrochloric acid." The results thus obtained are valuable for comparative purposes and serve to indicate, in a general way, the capacity of the stomach to secrete acid under standard conditions. This method has not been generally applied to the study of the gastric secretion of infants, as it is more difficult of application and the results obtained do not give the information desired.

A method which is easily applied and which gives information of greater significance consists in the determination of the concentration of the hydrogen ions in the gastric contents at the height of digestion. It is the free hydrogen ions which are responsible for the characteristic properties of all acids. The effective "strength" of any acid solution may be expressed in terms of the number of grams of ionized hydrogen present in solution. A normal solution of hydrochloric acid contains approximately 1 gm. of ionized hydrogen per liter; a tenth normal solution, 0.1 gm. ionized hydrogen, and a millionth normal solution, 0.000001 gm. In order to simplify the expressions and to avoid the use of many ciphers, it is customary to use logarithmic terms with negative exponents and indicate a tenth normal solution of acid as having a hydrogen-ion concentration of 10^{-1}, a millionth normal solution as 10^{-6}, or more simply as p_H 1, p_H 6, etc.

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* From the Department of Pediatrics, Washington University School of Medicine, and the St. Louis Children's Hospital.

* A preliminary report on this work was read before the American Pediatric Society, Washington, D. C., May 1, 1922. Marriott, W. McK.; Davidson, L. T., and Harshman, L. P.: Studies on the Digestion in Infancy, Proc. Am. Pediat. Soc. **34**:39-45, 1922.

As the action of hydrochloric acid in the processes of digestion is largely, if not entirely, due to the number of free hydrogen ions present, the determination of the hydrogen-ion concentration is of more significance than the determination of the total gastric secretion by titration methods. Various foods, especially milk, as will be seen later, have the property of binding large amounts of acid and converting the hydrogen into a nonionized form, thus to all intents and purposes neutralizing the acid. When foods of the type mentioned are given, much of the hydrochloric acid secreted is rendered inactive; hence, if one is to gain an idea of the effective acid concentration, it is necessary to determine the hydrogen-ion concentration at the height of digestion following a regular feeding. This method gives one a true idea of conditions actually present in the stomach at the time when the customary food is being digested. For practical purposes, this information is of more value than that obtained by titration methods applied to gastric contents obtained after other than customary feedings.

In our work, we have removed the gastric contents from infants at the height of digestion and have determined the hydrogen-ion concentration by means of the simple dialysis-indicator method,[1] which has been shown to yield results closely approximating those obtained by the electrometric method.

TECHNIC

Gastric contents were removed by means of a soft rubber catheter and a syringe. The catheter was introduced through the mouth or the nose. It was found that this could be done by an experienced person without causing much discomfort to the infant. Whenever violent retching, vomiting or the outpouring of large amounts of mucus occurred, the attempt to obtain gastric contents was abandoned until the following day, as otherwise the results were not reliable because the alkaline mucus partly neutralizes the acid present. Gastric contents were removed two hours after a feeding. It was found that the acidity of the chyme reached a maximum within one and a half hours after a feeding, and maintained this maximum acidity for about an hour. It was found that more uniform results were obtained on contents removed at the end of two hours than at any other period after the feeding. With one or two exceptions, all infants studied were on a four-hour feeding interval.

When the conditions mentioned were fulfilled, it was found that determinations made on the same infant on successive days were regularly in close agreement. Whenever possible, a number of determinations were made on each infant. In determining the hydrogen-ion concentration of the samples, small portions were first tested with indicators to obtain the approximate p_H. Three c.c. of the contents was then placed in a clean collodion sack and dialyzed against 3 c.c. of

1. Levy, R. L.; Rowntree, L. G., and Marriott, W. McK.: A Simple Method for Determining Variations in the Hydrogen-Ion Concentration of the Blood, Arch. Int. Med. **16**:389 (Sept.) 1915.

physiologic sodium chlorid solution for fifteen minutes. The collodion sack was then removed and 6 drops of appropriate indicator added to the dialysate, which was then compared with the standard buffer solution, containing indicator. Approximately correct readings were possible by comparison with the color chart in Clark's book, but this was checked in all cases by comparison with buffer standards made up according to the description of Clark. The indicators used were thymol blue (p_H 1.2-2.8), brom phenol blue (p_H 3.0-4.6), methyl red (p_H 4.6-6.0) and brom cresol purple (p_H 5.8-6.8).[2]

THE GASTRIC ACIDITY OF NORMAL INFANTS FED ON BREAST MILK

The gastric contents of forty-one normal infants under 1 year of age were studied. Of these, twenty-three were fed at the breast and seventeen were receiving breast milk from the bottle. All were fed at four-hour intervals. The results obtained are plotted graphically in Chart 1, first column. Each dot represents the p_H of the gastric contents of an individual infant. When more than one determination was made, the results were averaged.

It will be seen from the chart that in over two-thirds of the gastric contents studied the p_H fell between 3 and 4. The average for the whole series was 3.75, this figure being in close agreement with that obtained by Davidsohn,[3] who, using the electrometric method, found an average p_H of 3.8 for a series of normal breast-fed infants. Other observers have obtained results, some of which varied considerably from the foregoing. These variations are to be explained by differences in the technic employed. A summary of previous results obtained is given by Davidsohn.[4]

THE GASTRIC ACIDITY OF ABNORMAL INFANTS FED ON BREAST MILK

In order to determine the effect of the infant's nutritional condition and the effect of the presence of infections on the acidity of the gastric contents, a group of sixteen infants was studied. These infants were all hospital patients, most of them extremely undernourished. These infants and others in the series were suffering from acute and chronic infections, including otitis media, pyelitis, pneumonia, osteomyelitis and bacillary dysentery. The ages of the infants varied from 3 weeks to 9 months. The majority were between 3 and 5 months of age. All

2. For further details of the technic, the reader is referred to Clark, W. M.: The Determination of Hydrogen-Ions, Baltimore, Williams & Wilkins Co., 1920; and Levy, Rountree and Marriott: Footnote 1.

3. Davidsohn, H.: Arch. f. Kinderh. **69**:239 (April) 1921.

4. Davidsohn, H.: Arch. f. Kinderh. **69**:142 (April) 1921.

were receiving breast milk in amounts customary for the age. The results obtained are plotted graphically in Chart 1, second column. It will be seen that the p_H of the gastric contents of most of these infants varied between 4.4 and 4.8. All had a p_H above 4. The average for the series was 4.74. As we are dealing with negative exponents, this result indicates that the actual concentration of hydrogen ions in the stomachs of these sick infants at the height of digestion averaged only one-tenth as much as that of normal infants receiving the same food. There was a definite deficiency in the gastric secretion. In a number of instances, it was possible to study the same infants, first while normal, and subsequently when suffering from an infection. There

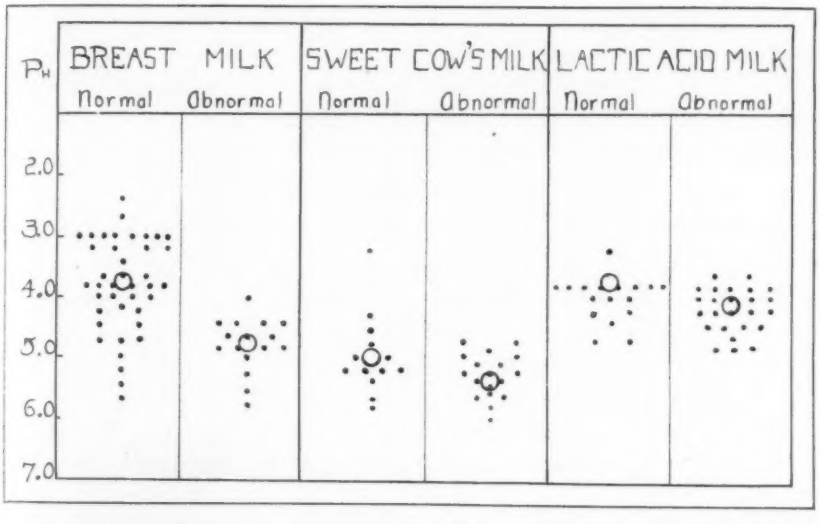

Chart 1.—Hydrogen-ion concentration of the gastric contents of infants. Each dot represents the average p_H for an individual infant. The circle represents the average for each group.

was regularly a marked decrease in gastric acidity in the presence of infection. The further significance of this lowered gastric acidity will be discussed subsequently.

THE INFLUENCE OF THE CHARACTER OF THE FEEDING ON THE GASTRIC ACIDITY

When cow's milk is added to an acid, a portion of the hydrogen of the acid is converted into a nonionized form, and the true acidity of the solution is thus greatly reduced. This is due to the fact that cow's milk contains a large amount of "buffer" material; that is to say, substances capable of uniting with considerable amounts of acid or alkali without undergoing a great change in chemical reaction. In cow's

milk, the chief buffer substances are the phosphates and the calcium caseinate. Of the total buffer substances present, approximately one-third exists in the whey and the remaining two-thirds in the curds. Human milk contains a smaller amount of buffer material, and, therefore, does not convert as much of the hydrogen of the acid into a nonionized form.

The effect of adding varying amounts of tenth normal hydrochloric acid to breast milk and to cow's milk are illustrated in Chart 2. On referring to the curves, it will be seen that, although cow's milk has an initial acidity slightly greater than that of breast milk, the addition of such an amount of hydrochloric acid as 30 c.c. of tenth normal acid

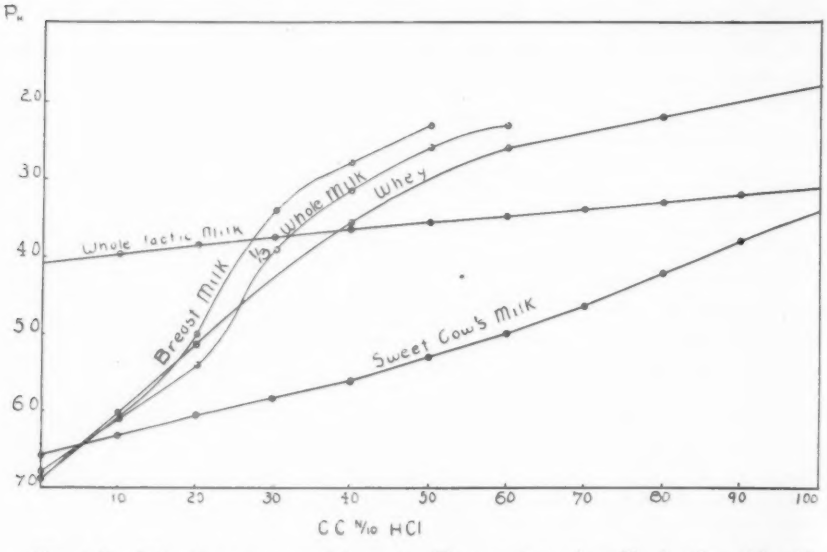

Chart 2.—Titration curves of breast milk, sweet cow's milk, lactic acid milk, diluted cow's milk and whey.

to 100 c.c. of milk results in a relatively slight change in hydrogen-ion concentration (p_H 6.6-5.85); whereas, the addition of the same amount of acid to breast milk changes the hydrogen-ion concentration to a much greater extent (p_H 6.9-3.4). In order to bring cow's milk to a p_H of 3.4, over 100 c.c. of acid is necessary, or approximately three times as much as in the case of breast milk. Judging from these results, one would expect that, when cow's milk was fed to an infant, the hydrogen-ion concentration at the height of digestion would be less than when an equal amount of breast milk was fed. This was found to be the case.

THE GASTRIC ACIDITY OF NORMAL INFANTS FED ON COW'S MILK

On feeding undiluted cow's milk to a group of the normal infants whose gastric acidity on breast milk feeding had been studied, it was found that the average p_H at the height of digestion was 5.3. This

means an effective concentration of acid of less than one-twentieth that in the case of the breast-fed infants. To another group of normal infants accustomed to cow's milk, the average hydrogen-ion concentration following a meal of undiluted whole cow's milk was 4.75. From this, it would appear that infants fed on cow's milk gradually adapt the gastric secretion to this type of food in such a way that a greater amount of hydrochloric acid is secreted by the stomach, and this partially, though by no means completely, overcomes the effects of the buffer substance.

The results of the feeding of undiluted whole milk to normal infants are presented graphically in Chart 1, third column. The average for the whole series was 5.1. One infant studied was not included in this series because of the unusual character of the preceding feeding. This infant, 4 months old, had been fed on large amounts of undiluted cow's milk for three months. The gastric acidity in this case was p_H 3.3. This finding accords well with the assumption that the feeding of cow's milk ultimately results in a compensatory increase in gastric acidity.

THE GASTRIC ACIDITY OF ABNORMAL INFANTS FED ON COW'S MILK

In feeding undiluted cow's milk to malnourished infants and those suffering from acute infections, it was found that the gastric acidity at the height of digestion was less than in any other series of infants studied. Sixteen of the abnormal infants whose gastric contents on breast milk feeding had been determined were fed on undiluted whole milk. The average p_H at the height of digestion was 5.35. The results appear in graphic form in Chart 1, fourth column.

THE GASTRIC ACIDITY OF NORMAL INFANTS FED ON LACTIC ACID MILK

Lactic acid milk, containing from 0.5 to 0.7 per cent. of lactic acid, prepared by the action of lactic-acid-producing organisms, or by the addition of lactic acid to whole milk, has a considerable portion of its buffer substance neutralized by the lactic acid present. The titration curve of such milk with hydrochloric acid appears in Chart 2. From the chart, it will be seen that the addition of 30 c.c. of tenth normal hydrochloric acid to 100 c.c. of lactic acid milk leads to a hydrogen-ion concentration very close to that obtained when the same amount of hydrochloric acid is added to breast milk (p_H 3.6-3.8). As this is the average hydrogen-ion concentration of the gastric contents of normal infants fed on breast milk, one would expect that if lactic acid milk were fed in the same amounts to normal infants, the same hydrogen-ion concentration would be attained at the height of digestion.

Undiluted whole lactic acid milk was fed to seventeen normal infants, most of whom had already been studied with breast milk feeding. The average hydrogen-ion concentration was found to be 3.71, as compared with 3.75 in the case of breast milk. The results appear in graphic form in Chart 1, fifth column.

THE GASTRIC ACIDITY OF ABNORMAL INFANTS FED ON LACTIC ACID MILK

Referring again to the titration curve of whole lactic milk in Chart 2, it will be seen that the curve is a flat one, and that the hydrogen-ion concentration varies within narrow limits, even with considerable variations in the amount of acid added. This milk has a p_H approximating 4 before any acid at all is added. From these facts, one would expect that the feeding of lactic acid milk to abnormal infants with deficient gastric secretion would result in a fair degree of acidity of the gastric contents at the height of digestion, and this was found to be the case.

TABLE 1.—*Hydrogen-Ion Concentration (p_H) of Gastric Contents of Normal Infants and Those Suffering From Infections or Nutritional Disturbances, Fed on Breast Milk, Sweet Cow's Milk and Whole Lactic Acid Milk*

	Breast Milk	Cow's Milk	Acid Milk
Normal	3.75	5.1	3.71
Abnormal	4.74	5.35	4.1

Twenty-six infants suffering from severe malnutrition and infections were studied. Most of the infants in this group were previously studied to determine the effect of feeding breast milk. The results appear in graphic form in Chart 1, sixth column. The average p_H at the height of digestion was 4.1, or somewhat more acid than in the case of the same group of infants fed on breast milk. This figure closely approximates the p_H of the gastric contents of normal breast-fed infants.

A summary of the gastric findings in normal and abnormal infants fed on various types of foods appears in Table 1.

THE SIGNIFICANCE OF THE GASTRIC ACIDITY

The acid of the gastric contents when present in large enough amounts to lead to a sufficient concentration of hydrogen ions performs a number of functions.

A certain hydrogen-ion concentration is necessary in order for peptic digestion of protein to occur. It has been found that peptic digestion begins at p_H 4 and is optimum at p_H 2.[5] From the results

5. Sørensen, S. P. L.: Biochem. Ztschr. **21**:131, 201; **22**:352, 1909.

which we have obtained, it is apparent that some peptic digestion was possible in over two thirds of the normal breast-fed infants examined and in a fair number of the infants fed on lactic acid milk. No peptic digestion was possible in the case of the infants suffering from nutritional disturbances or infections whether fed on breast milk or sweet cow's milk. It was possible, however, in a fair proportion of the sick infants fed on lactic acid milk. Even in the case of normal infants fed on sweet cow's milk, the hydrogen-ion concentration was insufficient for any peptic digestion.

It is difficult to estimate the importance of peptic digestion in infancy. Certainly, a considerable portion of the protein of the food passes the pylorus without having undergone any digestion, even under normal conditions, and it may be argued that all of the protein could escape peptic digestion without any disadvantage to the infant. On the other hand, it has been shown that the peptones resulting from peptic digestion are capable of stimulating the flow of pancreatic juice and bile,[6] and even the small amount of peptone formed might very well function in this way.

A rennin action on casein occurs at a lesser degree of gastric acidity than does peptic digestion. Casein is well coagulated by rennin at p_H 5.[5] With a lesser degree of acidity, the passage of unchanged casein past the pylorus is favored. The recent observations of Schloss and Anderson[7] on the passage of unchanged protein through the intestinal wall of athreptic infants suggests that denaturization of the casein by rennin coagulation may be of importance in preventing such absorption. The acidity of the gastric contents is known to regulate in some measure the pyloric reflex and gastric motility. Cowie and Lyon[8] have demonstrated that either an excess or a deficiency of acid leads to a prolonged emptying time of the stomach. Our own observations have been that, in general, a larger portion of the feeding was present, and could be removed by a catheter at the end of two hours, in the case of infants with a deficiency in gastric acidity than in those with an acidity approximating that of normal breast-fed infants. We do not believe, however, that the degree of acidity is the only factor influencing the gastric motility in such infants.

An important function of the acid of the gastric juice is its antiseptic action. It has been shown that, at p_H 5, marked inhibition of the growth of members of the colon, dysentery and typhoid group of bacilli occurs, and that at p_H 4 complete inhibition or death of the

6. Flieg, C.: Arch. Internat. d. Physiol. **1**:286, 1904.
7. Schloss, O. M., and Anderson, A. F.: Proc. Am. Pediat. Soc., 1923.
8. Cowie, D. M., and Lyon, W.: Am. J. Dis. Child. **2**:252, 1911.

organisms takes place.[9] It appears probable from the work of Bessau and Bossert[10] that invasion of the duodenum with members of the colon group of bacteria is a contributory factor in the production of diarrhea and nutritional disturbances of infants. A sufficient degree of acidity of the gastric contents such as occurs in normal breast-fed infants or in infants fed on lactic acid milk greatly decreases the chance of infection of the upper intestine with potentially harmful bacteria.

A further function of the acid in the gastro-intestinal tract is a stimulation of the flow of pancreatic juice, bile and intestinal secretions. This fact is noted when the acid chyme pours into the duodenum and is, according to Bayless and Starling, due to the production in the intestinal mucosa of the hormone "secretin." As acids other than hydrochloric acid have the same affect in stimulating the flow of these digestive juices,[6] it is evidently the hydrogen ion which is the active agent. Such being the case, a sufficient degree of acidity of the gastric contents must be an important factor in favoring subsequent intestinal digestion.

It was found by Klotz[11] that the addition of moderate amounts of lactic acid to the food of infants results in distinctly better absorption of all food elements from the gastro-intestinal tract. In these experiments, the amount of acid most favorable in its affect was just about sufficient to neutralize the buffer substances to such an extent as to lead to a normal gastric acidity.

From the foregoing considerations, it is evident that the acidity of the gastric contents may play an important rôle in the general processes of digestion and in the nutrition of infants. The experimental results recorded in the first part of this paper show that marked variations in gastric acidity occur and that, in general, a decrease in acidity is likely to be associated with nutritional and gastro-intestinal disturbances.

MEANS OF ALTERING THE GASTRIC ACIDITY OF INFANTS

The acidity of the gastric contents of an infant at the height of digestion may be low as the result of insufficient secretion of acid or as the result of administration of food of such high buffer value that the acid secreted is neutralized. When the gastric secretion is deficient, it may be the result of disease or malnutrition. In such instances, treatment directed toward the underlying condition usually results in an improvement in secretion. We have, however, at present no effective specific means of increasing the gastric secretion.

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9. Shohl, A. T., and Janney, J. H.: J. Urol. **1**:211 (April) 1917. Ohta, K.: Jahrb. Kinderh. **85**:358, 1917.
10. Bessau and Bossert: Jahrb. f. Kinderh. **89**:213, 1919.
11. Klotz: Jahrb. f. Kinderh. **70**:1, 1909.

The acidity of the gastric contents at the height of digestion may be increased to a considerable extent by proper choice of food as regards buffer value. Breast milk has a low buffer value and can be fed in larger amounts than cow's milk. The feeding of diluted cow's milk is equivalent to feeding of a lesser total amount of milk, and there is, consequently, less neutralization of gastric acid. The feeding of cow's milk in 1 : 3 dilution leads to approximately the same concentration of acid at the height of digestion as when the same amount of breast milk is fed. The acid titration curve of 1 : 3 cow's milk is plotted in Chart 2, and from this it will be seen that such diluted milk reacts with acid in about the same manner as does breast milk. In the customary modifications of cow's milk for infant feeding the milk is diluted and the buffer substance thus proportionately reduced. These mixtures, and also whey (Chart 2) lead to fairly normal conditions of acidity in the gastric contents, but, unfortunately, do not supply sufficient food value as measured by calories. The additions made to such mixtures are usually carbohydrates, or cream, the former having no buffer value and the latter very little. Another means of reducing the buffer value of milk is by drying. In this process, a portion of the calcium and phosphate is converted to insoluble tribasic calcium phosphate, and to this extent the buffer substances are reduced.

Another method of eliminating the buffer substances of milk is to saturate the buffer with acid. This is equivalent to augmenting the acid of the gastric juice. Hydrochloric acid would appear to be the natural acid to add, and certainly, as far as conditions in the gastrointestinal tract are concerned, it would be ideal. Unfortunately, however, only limited amounts of hydrochloric acid can safely be added to the food of an infant because of the fact that this acid is not destroyed in the body, but must be eliminated; and this throws a rather severe strain on the acid-base regulating mechanism and may lead to acidosis. Faber [12] has recommended the use of a small amount of hydrochloric acid, not sufficient to saturate the buffer, and even this amount has been shown by him to render the cow's milk more suitable as a food for infants.

Organic acids are not open to the same objections as is hydrochloric acid, since these acids can be completely oxidized in the body. Lactic acid serves very well to neutralize the buffer of cow's milk. It is, furthermore, in reasonable amounts, free from any harmful effects. Acetic, citric and butyric acids tend to cause diarrhea. Certain other organic acids, such as oxalic, are definitely toxic, and others, although possibly suitable from the physiologic standpoint, are difficult to obtain.

12. Faber, H. K.: Proc. Am. Pediat. Soc., 1923.

Everything considered, lactic acid is the acid of choice. It is an interesting coincidence that the amount of lactic acid ordinarily found in buttermilk, or lactic acid milk, is just sufficient to saturate the buffer substances of milk to such an extent that the additional acid required to bring the hydrogen-ion concentration to the normal average of gastric contents (p_H 3.8) is exactly the same as in the case of breast milk (Chart 2).

It has been known for many years that infants could usually tolerate larger amounts of sour than of sweet cow's milk, and it seems probable from the foregoing considerations that this increased tolerance is largely the result of the attainment of optimum conditions of acidity in the gastro-intestinal tract. In our experience, as good results are obtained on feeding sterile cow's milk acidified by the addition of lactic acid (from 0.5 to 0.7 per cent.). Such milk may be fed undiluted to even

TABLE 2.—*Comparative Effects of Feeding Infants on Sweet Cow's Milk, Bulgarian Milk and Milk Acidified by the Addition of Lactic Acid*

		Bulgarian Milk			Acid Milk			Sweet Milk		
Case	Age	Days Fed	Total Gain, Gm.	Daily Gain, Gm.	Days Fed	Total Gain, Gm.	Daily Gain, Gm.	Days Fed	Total Gain, Gm.	Daily Gain, Gm.
1	5 days	10	360	36	14	540	38	12	250	21
2	2 weeks	30	900	30	17	600	35	14	200	11
3	2 weeks	16	600	37	14	800	57	7	220	30
4	4 weeks	21	600	28	14	580	41	5	120	24
5	4 weeks	14	560	40	12	560	47	16	410	25
6	8 weeks	12	400	33	14	450	32	14	150	11
7	8 weeks	28	900	32	7	250	36	8	150	20
8	10 weeks	7	350	50	17	850	50	16	550	34
9	10 weeks	12	500	42	18	500	28	8	0	0
10	16 weeks	14	400	21	17	600	35	9	0	0
Average.....				35			40			16

young babies without leading to the nutritional or digestive disturbances that so commonly occur when whole sweet cow's milk is fed undiluted. This method of rendering milk digestible possesses a distinct advantage over the dilution method in that considerably more milk, and consequently a larger amount of food, may be administered.

The favorable effect on the nutrition of acidification of cow's milk is well shown in a series of feeding experiments which we have carried out. Ten young infants in the wards of the hospital were fed for varying lengths of time on each of three diets; whole sweet milk, bacterially soured whole milk and whole milk acidified by the addition of 0.6 per cent. lactic acid. Sugar in the form of corn syrup was added to the milk in every instance. Each infant received the same amount of milk and of sugar during each period. The order in which the feedings were alternated was varied in the case of different infants. There were no digestive disturbances in any of the infants whether fed on bulgarian milk or on acidified milk. In a number of instances, how-

ever, diarrhea or vomiting occurred while the infants were taking the sweet milk. These symptoms disappeared on the resumption of acid milk feedings.

The results are summarized in Table 2.

It will be seen that the gain in weight was distinctly greater during the periods of feeding of one of the lactic-acid-containing milks, than during the sweet-milk periods. These observations have been amply confirmed in the case of several hundred infants in the hospital and clinic who have been fed on lactic acid milk for long periods of time. There has been regularly a more striking gain in weight and a lesser incidence of gastro-intestinal disturbances among this group of infants than among those fed on sweet-milk formulas. A more detailed discussion of the use of whole lactic acid milk appears elsewhere.[13]

We have rarely observed an excessive secretion of gastric acid in infancy, and we have seen no symptoms that could be attributed to excessive acidity of the gastric contents. It is possible, however, that some infants may suffer from hyperchlorhydria. In such infants, food with a high buffer value would be theoretically indicated.

SUMMARY AND CONCLUSIONS

1. The acidity of the gastric contents of a group of normal breast-fed infants at the height of digestion averaged p_H 3.75.

2. The acid normally present is sufficient to perform a number of important functions. Any considerable decrease in the amount of acid is likely to be associated with digestive disturbances.

3. The acidity of the gastric contents of infants suffering from infections or nutritional disturbances is distinctly lower than that of normal infants.

4. Sweet cow's milk, by reason of its high "buffer" value, is capable of neutralizing a considerable portion of the acid of the gastric juice. This is one important reason why large amounts of sweet cow's milk cannot be well tolerated by infants.

5. Milk containing from 0.5 to 0.7 per cent. of lactic acid does not neutralize the acid of the gastric juice to any greater extent than does breast milk. When such milk is fed undiluted to infants, the acidity of the gastric contents approximates that of normal breast-fed infants. It is probable that, for this reason, infants are able to tolerate large amounts of lactic acid milk.

6. In selecting a food for young infants, it is important to take into consideration the "buffer" or acid-binding qualities.

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13. Marriott, W. M., and Davidson, L. T.: J. A. M. A., to be published.

PHYSIOLOGY OF EXERCISE

PART 3. AN INVESTIGATION OF CARDIOVASCULAR TESTS IN NORMAL CHILDREN AND IN CHILDREN WITH TUBERCULOSIS AND VALVULAR HEART DISEASE*

MAX SEHAM, M.D., AND GRETE EGERER-SEHAM, PH.D.

MINNEAPOLIS

In an investigation of the physical efficiency of schoolchildren, over a period of three years, we were impressed by (1) the high percentage of physically defective children; (2) the admission to school of physically subefficient children; (3) the inadequacy of the present system of physical examinations for the recognition and classification of abnormal conditions, and (4) the great need of objective methods for determining physical efficiency; the medical profession must admit that a mere anatomic basis for classification of disease is inadequate for this purpose.

Methods to determine physical efficiency are necessarily subjective, objective, or both. The subjective method concerns itself with an accurate history of the reaction of a person to his daily activities. Regarding objective methods, the literature in clinical medicine may be divided into two groups: (1) the quantitative measurement of capacity for physical work and (2) the reaction of the circulatory system to changes in posture and to measured amounts of work. This paper will limit itself to the discussion of the second group.

For a better understanding of the physiologic principles upon which cardiovascular tests are based, the meaning of the terms "functional capacity" and "reserve of the heart" may be clarified by the following theoretical example.

In a child, 11 years of age, weighing 35 kg., there are about 2.1 liters of blood. Forty-five seconds is required for a complete circulation of this amount of blood. With a systolic blood pressure of, let us say, 100 mm. (the pressure of a column of blood of 1.35 meters $= \frac{(100 \times 13.5)}{1,000}$), the work of the left ventricle in one minute would equal $1.35 \times 2.1 \times 4/3 = 3.78$ kg.; in one day, therefore, 5,443 kg. It has been estimated that the right ventricle accomplishes about one third the amount of the work done by the left ventricle. Thus, at rest, the total output of the heart in twenty-four hours would be about 7,257 kg., as compared with about 14,000 kg. performed by the heart of the adult. Since, in violent exertion, the pulse rate can increase two times, and in times of emergency, the systolic blood pressure can rise

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* From the Department of Pediatrics of the University of Minnesota and the Lymanhurst Hospital.

about 50 per cent., the cardiac output may increase two and a half times. This increase, amounting to 5.67 kg. in emergency, represents the reserve of the heart. In severe exercise, the total output or the functional capacity of the heart for each minute would equal $3.71 \times 5/2 = 9.45$ kg.

The nearest approach to an accurate, quantitative measurement of the total output of the heart has been made in the laboratory, by Krogh,[1] in his studies of the minute volume and the circulation time; by Pearce,[2] in his attempt to establish a cardiorespiratory index, and by others who have measured the quantity of blood from the blood vessels directly. Such methods obviously cannot be applied in every day clinical medicine.

The other so-called cardiovascular tests (Herz,[3] Selig,[4] Katzenstein,[5] Gräupner,[6] Barringer,[7] Crampton,[8] Schneider[9]) are not functional capacity tests, but are merely records of either the effect of change of posture on the pulse rate and the blood pressure or the effect of exercise on the circulatory reactions or both.

EFFECT OF CHANGE OF POSTURE ON THE PULSE RATE AND THE BLOOD PRESSURE

Pulse Rate.—In 1833, Donnell[10] observed that the pulse rate was slower in the lying posture than in the standing. Gräupner claimed to have found that the normal difference in the pulse rate from the standing to the lying posture, from seven to fifteen beats per minute, is considerably lessened or altogether lost in valvular heart disease. Geigel[11] believed that a variation of the pulse rate above thirty beats indicated a weakened heart condition. Kahn[12] claimed the average difference of the pulse rate to be sixteen beats for normal hearts. The majority of clinicians accept twenty beats as the limit of normal variation.

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2. Pearce, R. G.: Cardiorespiratory Mechanism in Health and Disease, Arch. Int. Med. **29**:139 (Feb.) 1921.
3. Herz: Lehrbuch der Heilgymnastik, Wien, 1904, Deutsch. med. Wchnschr. **31**:215, 1905.
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5. Katzenstein: Deutsch. med. Wchnschr. **30**:807, 1904; **41**:457, 1915.
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Blood Pressure.—All authors agree that recumbency decreases the pulse rate. The opinion varies, however, regarding the effect of change of posture on the blood pressure, owing, probably, to differences in technic and to the sensitiveness of the blood pressure mechanism. A difference in the size of the cuff produces a difference in the reading. Readings taken at different levels of the meniscus differ. The blood pressure is different at different times of the day in the same position, different before and after meals. Psychic influences cause a change in blood pressure as great as from 10 to 20 mm. (e. g., entrance of the school principal into the room increased the blood pressure from 10 to 15 mm.). The first reading is practically always higher than the successive readings. The systolic blood pressure in children is so elastic and so sensitive to artificial changes that it is practically impossible to apply with sufficient accuracy what seems to be normal standards to diseased conditions.

Some authorities find the blood pressure in the lying posture from 10 to 15 mm. higher than that in the standing; others find the pressure standing from 10 to 15 mm. higher than that taken lying. All, however, are agreed that a difference exists between the two in normal conditions.

Crampton's test based on the effect of change of posture on the pulse rate and the blood pressure is most commonly used in this country.

Crampton correlates the differences of blood pressure and pulse rate resulting from a change in posture. He did not base his correlations on a mathematical analysis of physiologic data, but arbitrarily assumed that a correlation exists. He believes that a rise in blood pressure with a change in posture is an index of physical efficiency. He states: "This test will not reveal more than it assumes to test, i. e., the efficiency of the vasomotor system. It will not show the presence of a mitral lesion. Nor will it test other factors of efficiency such as will power, inhibition or skill. It does provide a means of making a definite record of an all important function."

Crampton emphasizes the necessity for considering both factors, the blood pressure as well as the pulse rate. His scale therefore consists of two parts: (*a*) the increase of the heart rate, 0 to forty-five beats, subdivided in groups of five beats each, on changing from the reclining position to the erect, and (*b*) the increase of the blood pressure of 10 mm. above and below zero on change of posture; e. g., if in a subject the heart rate increases twenty-one beats and the blood pressure 4 mm. when changing from lying to standing, the subject is rated 60. The 100 mark indicates a perfectly efficient working of the vasomotor system; the lower the mark, the less the physical fitness.

This test, so easy of application, would be a great aid in the functional diagnosis of heart disease provided it was scientifically criticism proof. We, therefore, undertook an investigation of (1) normal children,[13] (2) children with tuberculosis and (3) children with heart disease. We compared the results obtained in normal children with those in children suffering from disease. We furthermore determined statistically the correlation of the changes in the blood pressure and the pulse rate following a change of posture.

In applying Crampton's test, it was necessary to change Part 2 in the scale; that is, the differences in the blood pressure in the lying and standing postures, because our blood pressure readings in the lying posture were almost invariably higher than in the erect (800 determinations on 300 children were made). Our limit of normal variation of the differences of the blood pressure was 0 to 20 mm. Crampton's scale for the pulse rates was retained. The test was applied to sixteen normal children, sixteen tuberculous children and sixteen with heart affections, including one who suffered from heart block. This number was considered sufficiently large to form a basis for conclusions. The average rating for the normal children was 68.2, with a maximum of 87 and a minimum of 25; that for the tuberculous children was 58, with a maximum of 90 and a minimum of 20; and the rating for the children afflicted with heart disease was 68, with a maximum of 102.5 (diagnosis: mitral regurgitation, first degree) and a minimum of 40 (diagnosis: mitral regurgitation, hypertrophy of the heart, second degree). If Crampton's original scale is applied without a change in the blood pressure figures, the rating would be as follows: The average for normal children equals 32.6 (maximum, 63; minimum, 3); the average for tuberculous children equals 42 (maximum, 65; minimum, 20), and the average for children with heart disease equals 33 (maximum, 62.5, in a case of mitral regurgitation, hypertrophy of the heart, second degree; and minimum, 15, in a child with mitral regurgitation. Table 1 shows in detail that Crampton's scale, whether modified or not, cannot be used in children for the functional diagnosis of such diseases as tuberculosis and heart disease.

In addition, the correlation of the differences in the blood pressure and the pulse rate in the lying and standing postures was calculated. Six hundred readings of the pulse rate and the blood pressure were taken on 102 normal children ranging from 6 to 15 years of age.

13. Seham, Max, and Egerer-Seham, Grete: Physiology of Exercise in Childhood. Part 1. A Study of Normal Children of School Age, Am. J. Dis. Child. **25**:1-45 (Jan.) 1923.

TABLE 1.—*Findings in Sixteen Cases*

	Normal				*Tuberculosis				Heart Disease				
Case	Pulse Rate St.-Ly.	Blood Pressure St.-Ly.	Cramp-ton	Scham	Pulse Rate St.-Ly.	Blood Pressure St.-Ly.	Cramp-ton	Scham	Pulse Rate St.-Ly.	Blood Pressure St.-Ly.	Cramp-ton	Scham	Diagnosis
1	+ 5	—11	45	72.5	— 2	— 8	55	70	+12	—14	30	75	Pulmonary stenosis
2	+10	—13	35	72.5	+ 4	— 7	62.5	67.5	+22	—26	15	70	Mitral regurgitation
3	+23	— 5	63	37.5	+14	—16	20	75	+ 4	—14	40	85	Mitral regurgitation; stenosis
4	+13	—12	30	65	+12	— 9	42.5	62.5	+17	—10	30	55	Mitral regurgitation; hypertrophy
5	+10	—13	32	72.5	+ 1	— 4	65	60	+ 9	—12	35	70	Mitral regurgitation
6	+ 8	—12	40	75	+ 9	— 8	45	60	+27	— 5	32.5	32.5	Unclassified
7	+19	—20	7.5	80	+26	0	45	20	+10	— 7	47.5	57.5	Congenital heart disease, first degree
8	+18	— 1	52.5	32.5	+12	— 6	50	35	+ 9	—11	37.5	67.5	Mitral regurgitation, stenosis, second degree
9	+26	—17	2.5	62.5	+21	—12	20	55	+13	— 9	37.5	57.5	Mitral regurgitation, first degree
10	+ 6	—12	40	75	+ 7	—18	25	90	+18	— 8	35	50	Mitral regurgitation, second degree
11	+21	0	55	25	+20	—11	37.5	57.5	+ 9.5	—10	40	65	Mitral regurgitation, first degree
12	+15	—11	32	62.5	+ 2	— 4	65	60+	12	—13	32.5	72.5	Possibly compensated mitral regurgitation
13	+12	—19	20	87.5	+11	—17	32.5	82.5	+ 7	—20	20	95	Mitral and aortic lesion
14	+13	—12	30	65	— 1	— 6	60	65	+ 1	—21	22.5	102.5	Mitral regurgitation, first degree
15	+ 8	0	37	45	—18	—13	22.5	62.5	+17	— 4	4.5	40	Mitral regurgitation, hypertrophy, second degree
16	+20	—11	27	57.5	+18	0	55	30	+ 7	— 3	62.5	57.5	Mitral regurgitation, hypertrophy, second degree
Average			34.4	67.3	....	....	45.3	59.5	.. .	. ..	31.1	65.7	

TABLE 2.—*Pulse Rate and Blood Pressure of One Hundred and Two Normal Children*

Case	Age, Years	Pulse Rate: Variation St.-Ly.	Pulse Rate: X*	Pulse Rate: X²	Blood Pressure: Variation Ly.-St.	Blood Pressure: Y†	Blood Pressure: Y²	Blood Pressure: XY‡
1	15	15	+ 4	16	19	+ 8	64	+32
2	15	12	+ 1	1	15	+ 4	16	+ 4
3	15	19	+ 8	64	20	+ 9	81	+72
4	15	21	+10	100	20	+ 9	81	+90
5	15	10	+ 1	1	7	— 4	16	— 4
6	14	11	0	0	21	+10	100	0
7	14	16	+ 5	25	13	+ 2	4	+10
8	14	22	+11	121	5	— 6	36	—66
9	14	26	+15	225	12	+ 1	1	+15
10	14	8	— 3	9	7	— 4	16	+12
11	14	1	—10	100	19	+ 8	64	—80
12	14	15	+ 4	16	6	— 5	25	—20
13	14	10	— 1	1	13	+ 2	4	— 2
14	14	10	— 1	1	8	— 3	9	+ 3
15	14	9	— 2	4	13	+ 2	4	— 2
16	14	8	— 3	9	17	+ 6	36	—18
17	14	15	+ 4	16	14	+ 3	9	+12
18	14	12	+ 1	1	11	0	0	0
19	14	6	— 5	25	22	+11	121	—55
20	14	7	— 4	16	12	+ 1	1	— 4
21	14	10	— 1	1	4	— 7	49	+ 7
22	13	19	+ 8	64	1	—10	100	—80
23	13	20	+ 9	81	18	+ 7	49	+63
24	13	8	— 3	9	5	— 6	36	+18
25	13	17	+ 6	36	11	0	0	0
26	13	26	+15	225	17	+ 6	36	+90
27	13	13	+ 2	4	9	— 2	4	— 4
28	13	6	— 5	25	6	— 5	25	+25
29	13	10	— 1	1	11	0	0	0
30	13	13	+ 2	4	5	— 6	36	—12
31	13	3	— 8	64	20	+ 9	81	—72
32	13	4	— 7	49	11	0	0	0
33	13	16	+ 5	25	11	0	0	0
34	13	10	— 1	1	4	— 7	49	+ 7
35	13	10	— 1	1	7	— 4	16	+ 4
36	13	—2	—13	169	7	— 4	16	+52
37	13	6	— 5	25	12	+ 1	1	— 5
38	12	14	— 4	16	19	+ 8	64	—32
39	12	19	+ 8	64	12	+ 1	1	+ 8
40	12	3	— 8	64	17	+ 6	36	—48
41	12	15	+ 4	16	16	+ 5	25	+20
42	12	8	— 3	9	8	— 3	9	+ 9
43	12	13	+ 2	4	4	— 7	49	—14
44	12	4	— 7	49	15	+ 4	16	—28
45	12	9	— 2	4	13	+ 2	4	— 4
46	12	8	— 3	9	19	+ 8	64	—24
47	12	18	+ 7	49	20	+11	1212	+77
48	12	9	— 2	4	4	— 7	49	+14
49	12	18	+ 7	49	2	— 9	81	—63
50	11	19	+ 8	64	4	— 7	49	—56
51	11	12	+ 1	1	19	+ 8	64	+ 8
52	11	13	+ 2	4	11	0	0	0
53	11	14	+ 3	9	14	+ 3	9	+ 9
54	11	30	+19	361	8	+ 3	9	—57
55	11	6	— 5	25	18	+ 7	49	—35
56	11	4	— 7	49	12	+ 1	1	— 7
57	11	4	— 7	49	15	+ 4	16	—28
58	11	16	+ 5	25	10	— 1	1	— 5
59	11	9	— 2	4	9	— 2	4	— 4
60	10	26	+14	196	6	— 5	25	—70
61	10	10	— 1	1	9	— 2	4	— 4
62	10	20	+ 9	81	8	— 3	9	+81
63	10	20	+ 9	81	19	+ 8	64	72
64	10	8	— 3	9	13	+ 2	4	— 6
65	10	18	+ 7	49	17	+ 6	36	—42
66	10	10	— 1	1	10	— 1	1	+ 1
67	10	6	— 5	25	8	— 3	9	—15
68	10	—1	—12	144	14	+ 3	9	—36
69	9	29	+18	324	11	0	0	0
70	9	18	17	49	13	+ 2	4	+14
71	9	11	0	0	9	— 2	4	0
72	9	8	— 2	9	9	0	0	0
73	9	1	—10	100	9	— 2	4	+20
74	9	11	0	0	11	0	0	0
75	9	9	— 2	4	7	— 4	16	+ 8
76	9	16	+ 5	25	6	— 5	25	—25
77	9	6	— 5	25	15	— 4	16	+20
78	9	12	+ 1	1	13	+ 2	4	+ 2

TABLE 2.—*Pulse Rate and Blood Pressure of One Hundred and Two Normal Children—(Continued)*

		Pulse Rate			Blood Pressure			
Case	Age, Years	Variation St.-Ly.	X*	X²	Variation Ly.-St.	Y†	Y²	XY‡
79	8	14	+ 3	9	10	− 1	1	− 3
80	8	15	+ 4	16	12	+ 1	1	+ 4
81	8	12	+ 1	1	7	− 4	16	− 4
82	8	4	− 7	49	8	− 3	9	+21
83	8	14	+ 3	9	8	− 3	9	− 9
84	8	7	− 4	16	12	+ 1	1	− 4
85	8	12	+ 1	1	15	+ 4	16	+ 4
86	8	25	+14	196	13	+ 2	4	+28
87	8	−2	−13	169	9	− 2	4	+26
88	8	−1	−12	144	11	0	0	0
89	7	5	− 6	36	10	− 1	1	+ 6
90	7	7	− 4	16	8	− 3	9	+12
91	7	11	0	0	7	− 4	16	0
92	7	12	+ 1	1	9	− 2	4	− 2
93	7	15	+ 4	16	15	+ 4	16	+16
94	7	4	− 7	49	11	0	0	0
95	7	7	− 4	16	14	+ 3	9	−12
96	7	9	− 2	4	4	− 7	49	+14
97	7	4	− 7	49	15	+ 4	16	−28
98	7	8	− 3	9	9	− 2	4	+ 6
99	6	2	− 9	81	10	− 1	1	+10
100	6	11	0	0	7	− 4	16	0
101	6	−1	−12	144	14	+ 3	9	−36
102	6	9	− 2	4	5	− 6	36	+12

* X, deviation of the differences of the pulse rates (standing minus lying).
† Y, deviation of the difference in systolic blood pressure (lying minus standing).
‡ XY, product of the paired differences of each case.

$$\text{Standard deviation of pulse rate (from exact mean)} = \frac{X^2}{N} = 6.733$$

$$\text{Probable error of pulse rate} = \pm 4.541$$

$$\text{Standard deviation of systolic blood pressure (from exact mean)} = \frac{Y^2}{N} = 5.037$$

$$\text{Probable error of blood pressure} = \pm 3.402$$

$$\text{Coefficient of correlation} = \frac{XY}{N \times Y} = 0.04242.$$

N, number of cases (102).

Table 2 presents the statistical calculation of these data. A study of this table shows definitely that the correlation between the differences of the pulse rate and the blood pressure on change of posture is negative (0.04242).

EFFECT OF CHANGE OF POSITION ON THE PULSE RATE AND THE SYSTOLIC BLOOD PRESSURE IN TUBERCULOUS CHILDREN AND CHILDREN WITH HEART DISEASE

Some observers claim that, in certain diseased conditions, the vasomotor tone is so reduced as to allow a state of "blood ptosis." This theory has been advanced as an explanation for supposedly abnormal changes of the blood pressure and the pulse rate on change of posture in chronic fatigue and in miscellaneous disease.

We studied the effect of posture on the pulse rate and the blood pressure in fifty children with tuberculosis and sixty-eight children with heart disease. The technic used was that described in Part 1 [18] of

this series. The results are tabulated in Table 3. The figures in column Pulse Rate represent the differences between the pulse rates in the standing posture and the pulse rates in the lying, those in column Blood Pressure represent the differences in the systolic blood pressure in the lying position and that in the standing.

TABLE 3.—*Effect of Change of Position on the Pulse Rate and the Systolic Blood Pressure (6-15 Years)*

Age, Years	Normal		Tuberculosis		Heart Disease	
	Pulse Rate	Blood Pressure, Mm.	Pulse Rate	Blood Pressure, Mm.	Pulse Rate	Blood Pressure, Mm.
15	15.4	14.7	4.0	7.0	8.5	11.5
14	10.0	12.3	14.0	16.0	14.2	10.2
13	11.2	9.7	9.8	5.1	10.0	10.5
12	11.6	12.2	15.0	11.5	8.7	11.5
11	12.7	11.8	10.5	17.0	17.5	12.3
10	13.0	11.6	10.0	7.8	6.5	12.2
9	12.1	10.3	....	10.0	4.0	10.0
8	9.2	10.3	10.5	9.0	12.5	11.5
7	9.2	10.2	....	....	....	12.0
6	10.0	9.0	....	....	13.5	10.0

It can be seen at a glance that there is little difference in the effect of change of posture on the circulatory reactions in different conditions. This is more clearly brought out in Table 4, which contains the averages, maximal, and minimal, of the differences of the pulse rates and of the blood pressures, respectively, for all ages. A change of posture (from lying to standing) increases the pulse rate 11.4 beats and reduces the blood pressure 11.2 mm. in normal children; 10.5 beats and 10.4 mm. in tuberculous children; 9.3 beats and 11.2 mm. in children with heart disease.

The average ratio of pulse rate standing: pulse rate lying, and the average ratio of blood pressure lying: blood pressure standing is practically the same in the above mentioned conditions.

TABLE 4.—*Average, Maximal and Minimal Findings in Normal, Tuberculous and Heart Conditions*

Condition	Pulse Rate			Blood Pressure		
	Averages for All Ages	Maximum	Minimum	Averages for All Ages	Maximum	Minimum
Normal	11.4	15.4	9.2	11.2	14.7	9.0
Tuberculosis	10.5	15.0	4.0	10.4	17.0	5.1
Heart disease	9.3	14.2	4.0	11.2	12.3	10.0

Schneider's Test.—Schneider's cardiovascular test is based upon changes in the circulatory reactions on change in posture and after exercise.

Schneider arbitrarily established a "scoring scheme" comprising six factors: (*a*) the heart rate while the subject is lying down; (*b*) the heart rate while the subject is standing; (*c*) the increase in the number

of beats in the pulse rate when the standing and reclining postures are compared; (*d*) the acceleration in the pulse rate after exercise; (*e*) the time taken by the pulse to return to normal, and (*f*) the rise or fall in the systolic blood pressure on standing. The scores for each of the six items range from + 3 to — 3. A perfect score is 18. For detailed information, the reader is referred to Schneider's article.[9] Schneider claims that his scoring scheme "recognizes that fatigue or derangement may be evidenced" in each of the six factors enumerated above. Schneider examined fifty-four aviators who were pronounced ailing and physically below normal by medical officers. Of these fifty-four subjects, only six had a score of 10 or better, while 88.8 per cent. had scores ranging between 9 and — 1. These figures, according to Schneider, seem to indicate that a score of 9 or less is "characteristic" of physically unfit men.

In another group of 150 patients, forty-six scored 9 or less. Medical examiners recorded abnormal conditions in thirty of the forty-six; that is, in 65.2 per cent. of the cases. In these subjects, Schneider's cardiovascular data ran parallel with the medical diagnosis.

In our study of normal children, tuberculous children and those suffering from heart disease, we necessarily had to modify Schneider's scale, because his observations were carried out on adults. Since the pulse rates vary with the age in childhood, we arranged a scale for the pulse rates starting with the lowest figure and ending with the highest found for each year. We then divided the differences into six groups according to Schneider. Sections B, D and E in Schneider's scale hold good for children of school age. We changed only the type of exercise, allowing the children to do ten full dumbbell swings (420 foot pounds). In section F, Schneider allots 3 points for a rise of 8 mm. or more in the blood pressure from the reclining posture to the standing, and — 1 point to a fall of 6 mm. or more. As mentioned before, in our series, no rise but almost invariably a fall of the blood pressure was observed. Therefore, all of our subjects would have to be rated in section F (— 1) if we apply the test literally.

Normal children: Three children, 12 years of age, and two children, 11 years of age, all in perfect physical condition, were rated according to Schneider's modified scale.

The three 12-year-old children scored + 1, — 1 and + 4 points, respectively. One child, 11 years old, received 5 points, the second, of the same age, 4 points; while, on repetition of the experiment, the latter received 0.

Because no data were available for the maximum rise and reaction time in tuberculous children and those afflicted with heart disease, we thought it advisable to compare just the four sections (A, B, C, and F).

On the basis of a perfect score of 12 points, the normal children, 12 years of age, received 0, 2 and 3 points, respectively, and the 11-year-old normal children were rated 0 and 3 points.

In three tuberculous children (aged 12 years), the rating was 5, 5 and 3, respectively, which is higher than in the normal children of the same age.

Three children (12 years old) with heart disease had the following scores: Case 1 (diagnosis: mitral regurgitation, vertical heart) 6 points; Case 2 (diagnosis: mitral regurgitation, myocarditis chronic, second degree) —2 points; Case 3 (diagnosis: mitral regurgitation, first degree) 3 points. We thus have a case of heart disease receiving a rating of six points, while a perfectly normal child rated 0. In general, children with tuberculosis and heart disease rated higher than normal children.

Barringer's Test.—In 1898, Gräupner first determined the effect of exercise on the pulse rate and the blood pressure in normal adults and in adults with valvular heart disease. He made the following observations:

1. An abrupt drop of the blood pressure after severe muscular exertion or a slight rise (10 mm.) followed by a quick fall to a level below the preexercise level is evidence of functional insufficiency of the heart.

2. If the blood pressure remains high after cessation of work, and then suddenly falls, it indicates fatigue of the heart muscle.

3. If the blood pressure after work is lower than before exercise and then slowly ascends to normal, it is also a sign of myocardial insufficiency.

In 1916, Barringer confirmed most of Gräupner's conclusions. In addition, he established another sign of so-called myocardial insufficiency: "the delayed rise." He found, in normal adults and later in subjects with heart disease, that, after sufficiently severe exertion, the maximum reading of the systolic blood pressure occurs at sixty seconds or later rather than shortly after exercise (within thirty seconds). This "delayed rise" he considered indicative of myocardial insufficiency in normal subjects as well as in heart disease. Wilson [14] confirmed Barringer's work in children.

In Part 1 of this series, the circulatory reactions in normal children after exhaustive exercise were published. It was then stated that the maximum reading was obtained on an average at twenty-four seconds after cessation of work, only one delayed rise being obtained. The discrepancy between Barringer's and our results may lie in the fact

14. Wilson, M. G.: Circulatory Reactions to Graduated Exercise in Normal Children, Am. J. Dis. Child. **20**:188 (Sept.) 1920.

that we took our readings within from five to ten seconds after cessation of work and at periods of from five to ten seconds thereafter. Again, we did not feel justified in considering as secondary rises that were less than 3 mm. higher than the next highest reading, because changes in the blood pressure of 3 mm. lie within the limit of error. In Part 2 of this series, the circulatory reactions in collapse following exhaustive exercise were reported.[15] The curves of the pulse rate and the blood pressure show almost invariably an abrupt drop immediately after exercise, the first reading being as a rule the highest.

TABLE 5.—*Effect of Measured Amounts of Work Upon the Pulse Rate and the Blood Pressure (Thirty-Five Full Length Dumbbell Swings)*

	Normal						Heart Disease					
	Blood Pressure				Pulse Rate		Blood Pressure				Pulse Rate	
Age, Years	Maximum Rise, Mm.	Time Max. Reading, Sec.	Percentage of Recovery at 120 Sec.	Percentage of Recovery at 180 Sec.	Percentage of Recovery at 120 Sec.	Percentage of Recovery at 180 Sec.	Age, Years	Maximum Rise, Mm.	Time Max. Reading, Sec.	Percentage of Recovery at 120 Sec.	Percentage of Recovery at 180 Sec.	Percentage of Recovery at 120 Sec.	Percentage of Recovery at 180 Sec.
14.....	39	45	79.1	86.6	100	100	15.....	47	15	84.3	94.1	100	100
14.....	35	30	88.6	93.5	100	100	14.....	30	35	82.8	86.5	81.9	90
13.....	35	55	76.3	86.9	...	87.5	14.....	24	40	100	100	100	100
13.....	46	55	77.3	86.8	100	100	14.....	28	40	95	96.2	100	100
13.....	35	45	79.0	82.8	100	100	13.....	33	30	86.5	95.7	...	92
13.....	40	35	94.5	100	100	100	13.....	47	40	83.6	93.1	91	91
12.....	35	25	85.4	90.8	87.5	91.8	13.....	41	40	81.7	89.2	79.2	91.6
12.....	37	35	86.6	94.2	85.7	90	12.....	27	30	81.7	86.8	...	100
12.....	35	35	86.5	87.2	...	80	12.....	65	10	81.5	82.6	100	100
11.....	32	30	87.9	96.3	...	100	12.....	30	20	95.8	95.8	83.4	83.4
10.....	19	35	87.8	93.1	100	100	12.....	49	65	73.3	82.1	100	100
10.....	43	35	71.6	93.0	100	100	10.....	30	20	95.4	100.0	100	100
9.....	37	25	86.9	96.3	...	...	8.....	41	20	87.9	92.3	80	88.9
Average	41	39.4	83.4	91.3	97	95.5	Average	37.8	31.1	85.3	91.9	91.0	95.1

EFFECTS OF MEASURED AMOUNTS OF WORK ON THE PULSE RATE AND THE BLOOD PRESSURE

The opinion seems to prevail that in normal persons the circulatory reactions after exercise differ from those in subjects afflicted with heart disease, although equal amounts of work were performed.

To confirm or to refute this supposition, children between the ages of 8 and 15 years were studied. The first group consisted of thirteen normal children between the ages of 9 and 14; the second group of an equal number of children with heart disease, ranging between the ages of 8 and 15.

The exercise given consisted of thirty-five full length swings with two 4-pound dumbbells (only one child, 8 years old, swung a pair of 2-pound dumbbells). The technic described in Part 1 [13] was employed. The following items are tabulated in Table 5: (1) the maximum rise and

15. Seham, Max, and Egerer-Seham, Grete: Physiology of Exercise in Childhood. Part 2. Study of Collapse in Normal Children, Am. J. Dis. Child. **26**:254 (Sept.) 1923.

the time of maximum reading of the blood pressure (Columns 1 and 2); (2) the percentage recovery of the blood pressure at 120 seconds and 180 seconds, respectively (Column 3), and (3) the percentage recovery of the pulse rate after the same period of time (Column 4).

Comparing the results obtained in normal children with those obtained in children having heart disease, one is impressed by their similarity. The maximum rise of the blood pressure in children with heart disease is about 3 mm. lower than that in normal children. This certainly lies within the limit of error for blood pressure readings. The time of maximum reading is slightly lower in heart disease, 31.1 seconds as against 39.4 seconds in normals. The percentage recovery of the blood pressure amounts to 83.4 and 91.3, respectively, in normal children, and 85.3 and 91.9, respectively, for those with heart disease. The only difference lies in the percentage recovery of the pulse rate at 120 seconds, that for normal children being 97, as against 91.0 for

TABLE 6.—*Effect of Maximum Dumbbell Exercise on the Blood Pressure*

	Rise, Mm.			Time of Reading, Seconds			Percentage of Recovery at 180 Seconds
	Average	Maximum	Minimum	Average	Maximum	Minimum	
Normal cases (50 subjects, ages 9 to 15)	47.5	105	10	39.9	53	20	86.8
Tuberculosis (30 subjects, ages 9 to 15)	33.6	49	21	38.5	75*	20	86.2
Heart disease (30 subjects, ages 8 to 15)	38.4	55	16	36.3	85†	15	89.0

* One delayed rise
† Two delayed rises in the same subject.

children with diseased hearts. This difference, however, cannot be considered sufficient to be of practical value in diagnosing myocardial sufficiency.

EFFECT OF MAXIMUM DUMBBELL EXERCISE ON THE SYSTOLIC BLOOD PRESSURE

Fifty normal children, thirty tuberculous children and thirty children with pathologic heart conditions were studied as to the effect of maximum work on the circulatory reactions by means of full length dumbbell exercise.[13] Table 6 shows that the maximum rise of the blood pressure was highest in normal children (45.7 mm.), probably owing to the larger quantity of work performed. In those having tuberculosis or heart disease, the maximum reading was 33.6 mm. and 38.5 mm., respectively. It is interesting to note that, in spite of the varying quantities of work performed by each individual group, the average time of the maximum reading of the blood pressure was practically the same (39.9, 38.5 and 36.3 seconds, respectively).

CONCLUSIONS

1. The so-called cardiovascular tests, in use today, do not measure the functional capacity of the heart.

2. Crampton's, Schneider's and Barringer's tests do not seem to be of value in the diagnosis of physical fitness or cardiovascular ability in tuberculosis and heart disease in children.

3. Delayed rises did not occur after exhaustive exercise, either in normal children or in those with tuberculosis or heart disease.

RÉSUMÉ OF THE LITERATURE ON SKIN DISEASES OF INFANTS AND CHILDREN (1920-1923) *

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The contributions to medical literature on the skin diseases of infants and children have been numerous the past three years. Those of real value or marking advance in our knowledge, however, have been few. It has been my purpose to include only these in this review. In some instances, it has seemed profitable to review articles published before the year 1920.

ECZEMA

The most interesting advancement in the skin diseases of infants and children has been the demonstration of the relationship of protein sensitization to eczema, one of the most common skin diseases of children.

Using the scratch method of applying the proteins, O'Keefe [1] found that 41 per cent. of the cases of eczema in bottle-fed infants and older children whom he tested gave a positive reaction to proteins. In forty-one cases of breast-fed infants with eczema, 61 per cent. gave positive cutaneous reactions.

In Schloss' [2] series of seventy-seven cases of eczema in infancy and childhood, 65 per cent. gave a positive reaction to the cutaneous protein test.

Sidlick and Knowles,[3] Engman and Wander [4] give similar proportions of reactions in infants and children with eczema, while Spohn [5] gives a higher percentage of positive reactions in a smaller number of children studied.

Shannon,[6] in 1921, demonstrated that egg protein passed through the mother's milk and could sensitize the nursing infant of mothers

* Received for publication, Sept. 6, 1923.
* From the Department of Pediatrics and Infectious Diseases, University Hospital, Dr. D. M. Cowie, director.

1. O'Keefe, E. S.: Boston M. & S. J. **183**:569 (Nov. 11) 1920; **185**:194 (Aug. 18) 1921.
2. Schloss, O. M.: Allergy in Infants and Children, Am. J. Dis. Child. **19**:433 (June) 1920.
3. Sidlick, D. M., and Knowles, F. C.: Value of Cutaneous Sensitization Tests Employed in Eczema and Papular Urticaria of Childhood, Am. J. Dis. Child. **23**:316 (April) 1922.
4. Engman, M. F., and Wander, W. G.: Application of Cutaneous Sensitization to Diseases of the Skin, Arch. Dermat. & Syph. **3**:223 (March) 1921.
5. Spohn, H.: Canad. M. A. J. **12**:461 (July) 1922.
6. Shannon, W. R.: Demonstration of Food Proteins in Human Breast Milk by Anaphylactic Experiments on Guinea-Pigs: Their Probable Relationship to Certain Diseases of Nursing Infants: A Preliminary Report, Am. J. Dis. Child. **22**:223 (Sept.) 1921.

who included egg in their diet. These infants suffered from eczema. Discontinuing the offending protein, he contends, caused a disappearance of the eruption occurring in these infants. He further passively sensitized a series of guinea-pigs to egg protein and then caused shock in them by injection of the breast milk of mothers on an egg diet.

Recently, Stewart,[7] using the uterine strip method of Dale, a more sensitive method of producing anaphylaxis in animals, was unable to produce shock in guinea-pigs previously sensitized to egg protein by injection of breast milk from mothers who included egg in their diet. These were mothers of infants who had eczema. The infants all showed cutaneous reactions on application of the egg protein to the skin. He concludes from his work that it is not yet possible to demonstrate that egg protein passes through the mother's milk and sensitizes the infant.

There seems to be an unquestioned relationship between protein sensitization and the eczema of infants and children. However, direct evidence of the allergic nature of infantile eczema has not been demonstrated in all cases.

That the sugar and fats are the offending constituents in the diet in certain cases of eczema cannot be denied. These probably do not act in an allergic manner. All we can say at the present time is that any of the essentials of the diet, protein, fat or carbohydrate in excess, seem to have an influence toward continuation of the eruption. Most workers in this field feel that the protein skin test furnishes useful information as to the treatment of each individual case. The protein to which the child shows a cutaneous reaction should be omitted from the diet. Otherwise, the offending protein should be altered, as infants sensitized to cow's milk protein improve on a diet in which the cow's milk protein has been denaturized in some way, as by pancreatization, boiling or peptonizing. Schloss [2] gives the following summary of his work, utilizing this principle in the treatment of eczema:

1. Treatment by eliminating the foods to which the patient reacts.

2. Treatment by immunization, viz., by feeding gradually increasing amounts of the offending protein or food until tolerance is established.

3. Treatment by desensitization; that is, by hypodermic injections of the protein to which the patient is sensitive.

The most valuable addition to the drug therapy of eczema is the crude coal tar method, described by White.[8] The prescription consists of crude coal tar 2, zinc oxid 2, cornstarch 16, petrolatum 16 gm. It is necessary, first, to mix the cornstarch and petrolatum, and next, to

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7. Stewart, H. C.: Excretion of Foreign Protein in Human Milk, Am. J. Dis. Child. **25**:135 (Feb.) 1923.

8. White, C. J.: Crude Coal Tar in Dermatology, Arch. Dermat. & Syph. **4**:796 (Dec.) 1921.

mix the zinc oxid and coal tar, combining these two products as the final thick black paste used in the treatment. This product or paste can be removed from the skin by warm olive oil or mineral oil. Probably its greatest disadvantage is the staining of clothes and bed linen. However, this stain can be removed without injury to the clothing and bed linen. White advises covering both sides of the stained portion of the fabric with lard. This is left on for one hour, and then the cloth is washed with soap and water. By this method, the stain can be entirely removed.

URTICARIA

Sidlick and Knowles [8] remark that cutaneous reactions are brought to light when various proteins are applied by cutaneous or intracutaneous tests to the skin of patients subject to urticaria. They tested twelve children having urticaria, and nine of the group reacted to one or more proteins. Three of the subjects were clinically cured. Four were markedly improved by omitting these proteins from their food. The remaining children failed to improve on the restricted diet. Schloss made cutaneous tests on sixty patients with urticaria following regularly the ingestion of some food. In only ten cases were the tests positive. In four cases, it was possible to demonstrate the exact relationship by feeding experiments or immunization. In the rest of the series of cases that showed cutaneous reactions, it was impossible to prove a causal relationship by elimination of the foods in question.

In this disease, as well as in eczema, Sidlick [8] and Knowles remark that correcting the gastro-intestinal abnormalities, if possible, as well as eliminating the offending proteins from the diet, increases the number of clinical cures.

Walker [9] reports five cases of urticaria in children, two of which were caused by horse dander protein and three by ragweed pollen. Treatment by desensitization was satisfactory in these cases.

The occurrence of eczema, urticaria and asthma in the same child has been observed several times. The relationship of food sensitization to urticaria is now definitely established. The method of obtaining clinical improvement in urticaria is the same as that which is given under the outlined treatment for eczema.

PSORIASIS

Jamieson [10] studied the blood nitrogen in fifteen cases of psoriasis. He could not demonstrate any appreciable change in the blood urea

9. Walker, I. C.: Eczema from Proteins, J. A. M. A. **70**:897 (March 30) 1918.

10. Jamieson, R. C.: Experimental Work on Blood Nitrogen in Psoriasis, Arch. Dermat. & Syph. **4**:622 (Nov.) 1921.

nitrogen or uric acid. There was no relationship between the total nitrogen of the blood and the presence or absence of the lesions in the patients studied.

Sachs [11] reports favorable results in the treatment of psoriasis with intravenous solution of sodium salicylate. The first injection he gave was 2 gm.; the second injection, 3, and the third injection, 4, which was the maximum dose. Four injections usually suffice. Bravo [12] reports good results with this method of treatment. He uses smaller doses. The first injection was 0.5 gm.; the second injection, 1, and the third, 1.5. He gradually increases the dosage by 0.5 gm. until the dose of 3 or 4 gm. is reached. The interval between the injections is three days.

RINGWORM

Rasch [13] mentions one type of ringworm known as tinea kerion. This is also described by Williams.[14] It is a deep seated, acutely inflammatory process which results in the formation of a rounded boggy, carbuncle-like tumor. The surface of the lesion is reddish or purplish, and is marked by numerous pinhead to split pea size pustules and gaping follicular orifices. The subcutaneous tissue is honeycombed and filled with purulent matter, small amounts of which can be squeezed out through the follicular openings. The tumors may be either single or multiple. They are extremely sensitive to pressure and may give rise to a considerable amount of pain. In addition, there may be pronounced subjective symptoms accompanied by a rise in temperature. As a result of a long continued inflammatory reaction, this type of the disorder may undergo a spontaneous cure.

Cultures have shown that the fungus causing the kerion may be any one of the several species of fungi. There does not seem to be any relationship between the variety of the fungus and the character of the skin eruption. Associated with the kerion, there is often an accompanying exanthematous eruption. The commonest form of the exanthem is an eruption of small lichenoid papules, sometimes occurring singularly, but usually grouped in patches of varying size. Other types of the exanthem have also been noted, such as vesicles, pustules and a scarlatinaform rash.

In patients suffering from kerion, the injection of trichophytin may produce an exanthematous eruption exactly like that occurring in the course of the disease. This eruption also fades as the kerion heals, and

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11. Sachs, O.: Wein. klin. Wchnschr. **34**:185 (April 21) 1921.
12. Bravo, J.: Brit. J. Dermat. & Syph. **34**:353 (Nov.) 1922.
13. Rasch, C.: Brit. J. Dermat. **32**:317 (Nov.) 1920.
14. Williams, C. M.: Lichenoid Tricophytide, Arch. Dermat. & Syph. **4**:353 (Sept.) 1921.

if there are any areas of tinea on the skin, these also heal with the fading of the eruption. The eruption is generalized, occurring on the extremities, body and face.

The first treatment offered is medication. In early cases, this method is efficacious. In more advanced cases, with larger areas involved, medical treatment does not give as successful results.

Elford,[15] also Giffen,[16] has obtained successful results in children who had small patches of ringworm eruption on the scalp. They recommend shaving the head, and then next applying tincture of iodin. The infected areas are then sprayed with ethyl chlorid; the head is covered with a clean cotton cap, and the parents are instructed to shampoo the child's head at night. Treatment is continued each day for two weeks, and then the treatment is modified, according to the apparent progress. The parents are cautioned against the use of any greasy substance or other medication to supplement this form of treatment.

Strickler [17] advises the use of vaccines in the treatment of ringworm. He uses a vaccine made from a grown culture of the trichophyton. This vaccine is used in gradually increased doses. Usually, three injections of the vaccine suffice. Strickler obtained successful results in fifteen children in whom the vaccine was used.

Sabouraud's roentgen-ray technic for the treatment of tinea of the scalp has been improved through the introduction of the Coolidge tube, by which the amount of rays absorbed can be measured with accuracy. Oliver,[18] Lane,[19] Knowles,[20] Graham [21] and Hazen [22] have aided in developing a successful technic for the roentgen-ray treatment of ringworm. They report very successful results with this form of therapy. It may be said that the roentgen-ray treatment of tinea tonsurans is probably the most efficient method of treatment.

IMPETIGO CONTAGIOSA

Knowles [23] divides the eruption of impetigo contagiosa into four types:

1. The common variety, in which the lesions dry up into a yellowish crust and are readily cured with the proper medication.

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15. Elford, W. P.: Brit. M. J. **1**:867 (June 26) 1920.
16. Giffen, M. W.: Brit. M. J. **1**:267 (Feb. 18) 1922.
17. Strickler, A.: J. Cutan. Dis. **33**:181 (March) 1915.
18. Oliver, E. L.: Boston M. & S. J. **174**:751 (May 25) 1916.
19. Lane, C. G.: Boston M. & S. J. **183**:673 (Dec. 9) 1920.
20. Knowles, F. C.: Pennsylvania M. J. **20**:337 (Feb.) 1917.
21. Graham, J. G.: Brit. M. J. **2**:563 (Sept. 23) 1922.
22. Hazen, H. H.: J. Cutan. Dis. **37**:307 (May) 1919.
23. Knowles, F. C., and Munson, H. G.: Institutional Epidemics of Bullous Impetigo Contagiosa, Arch. Dermat. & Syph. **7**:376 (March) 1923.

2. The pustular type, which is in close association with a hair follicle.

3. An outbreak of dime size lesions with yellowish brown or brownish crusts and inflammatory areola—ecthyma.

4. The bullous type, which is usually classified as pemphigus neonatorum.

The usual type of impetigo contagiosa is a disease of children. The bullous form in most instances occurs in infants. Because of the contagiousness of the bullous type of impetigo, this form of the disease is very liable to occur in epidemic form in institutions caring for infants. Numerous epidemics have been reported in the literature, the mortality varying from 30 to 50 per cent.

There has been much discussion regarding the etiologic organism in impetigo contagiosa, as to whether the causitive organism belongs to the staphylococcus or to the streptococcus group. Highman [24] states that the cause of the affection is the streptococcus. Flehme,[25] in fifty-five cases of impetigo contagiosa, which he investigated bacteriologically, found streptococci in pure culture or mixed with staphylococci, according to the age of the lesions. In every case, the organism was of the type *Streptococcus longus*. In man, it was possible, through superficial inoculation of the organism, to form typical lesions of impetigo contagiosa. The organisms were also recovered in pure culture from the lesions produced. In 15 per cent. of normal persons, Flehme was able to culture the streptococci from the skin. The streptococcus closely resembled the organism found in clinical impetigo contagiosa. The superficial inoculation of pure cultures of streptococci recovered from normal skin likewise produced a clinical impetigo lesion.

Flehme [25] believes that the cause of impetigo contagiosa is the attack on fertile ground of a large dose of impetigo streptococci. The normal skin appears to have a resistance to the organism. One may consider the impetigo streptococcus as a semiparasitic organism which, under certain circumstances and with a diminished resistance of the skin, leads to the formation of the disease. In epidemics, there may be an increased virulence of the organism, which overcomes the normal resistance of the healthy skin.

Farley and Knowles,[26] in an extensive study of the bacteriology of impetigo contagiosa, conclude that the streptococcus is the etiologic organism in the common type of the infection. These authors state that, with proper precautions and under proper conditions, streptococci may

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24. Highman, W. J.: Dermatology, New York, The Macmillan Company, 1921.

25. Flehme, E.: Dermat. Ztschr. **31**:111 (Sept.) 1920.

26. Farley, D. D., and Knowles, F. C.: Impetigo Contagiosa, Arch. Dermat. & Syph. **3**:753 (June) 1921.

be obtained from nearly all cases of impetigo contagiosa. If the streptococci are to be obtained on culture, it is necessary to take the material from an early and unruptured lesion. If this is not possible, the culture should be taken from the deep, redder parts of the skin, from which all crusts have been removed. The following strains of the streptococci were found: *Streptococcus pyogenes, Streptococcus anginosus, Streptococcus subacidus* and *Streptococcus fecalis.* Associated organisms, such as staphylococci, pseudodiphtheria bacilli, are either secondary or extraneous invaders. It is not possible to predict from the clinical lesion what type of the streptococcus will be found in the culture.

Nothing new has been added to the therapy of impetigo contagiosa. Ammoniated mercury is recognized as specific. An important detail in the treatment by ointments is bandaging of the affected parts. The bandaging keeps the ointment in constant approximation to the lesions, and the end-result is effected sooner.

Morrow [27] uses silver nitrate to abort the early lesions of impetigo. He recommends that the vesicles or pustules be ruptured with gauze and the base of the lesion covered with silver 20 per cent. nitrate solution. When crusts are present, these should be removed also and the underlying base treated with the silver nitrate solution. He uses the same strength silver nitrate solution in infants and reports the same uniformly good results.

SCLEREMA

Lieberthal [28] gives the following classification of sclerema, which has in general been accepted: (1) sclerema adiposum and (2) sclerema edematosum (scleredema or edema neonatorum).

Sclerema adiposum, which is of far rarer occurrence than sclerema edematosum, develops either in the first few days of life, in weakly premature infants with or without internal disease; or later, within the first few months, subsequent to "cholera infantum," enteritis, pneumonia or some other disease. All parts of the body may become affected, except the palms, soles, scrotum and chest. The disease begins as a rule on the lower extremities and rather creeps upward. Its distribution is symmetrical. The skin becomes firm and hard, tightly drawn and firmly united with the subcutaneous tissues and the other structures; in other words, perfectly immovable. The color of the diseased skin is pale, yellowish, waxy or bluish red. The skin feels cold. In an extensive case of sclerema, the infant's body feels like a frozen corpse. The affected parts show no swelling: they are diminished in volume. The extremities are very thin, and the skin gives the impression of being glued to the bone. Active and passive motions are

27. Morrow, H.: Impetigo Contagiosa, J. A. M. A. **69**:177 (July 21) 1917
28. Lieberthal, D.: J. Cutan. Dis. **36**:29 (Jan.) 1918.

impeded. The pulse is slow and weak, and respirations are shallow and labored. The temperature of the whole body is considerably lowered. The prognosis of these cases which begin in the first days of life is uniformly unfavorable. Within a few days, the disease terminates fatally. Histologically, the affected skin is found contracted, atrophic and anemic.

Sclerema edematosum (scleredema or edema neonatorum) is observed on the second to the fourth day, rarely later than the fourteenth, in prematurely born, weakly developed infants, and in some cases of congenital syphilis. The disease consists of an intensive edema, which begins as a rule on the feet and the calves of the legs, gradually spreading to the trunk and upper extremities, and, in extreme cases, even to the neck and to the face. The skin shows at the beginning the characteristic red tint of the new born or is cyanotic. With the increase of the edema, the skin appears either pale or more cyanotic. Pitting on pressure disappears slowly. In higher degrees of development, however, there is no pitting, the skin being firm and immovable. There is considerable increase in volume of the parts affected, which produces disfigurement and impedes motion. The skin feels cold and the body temperature is considerably reduced. The children are apathetic. The respirations are weak and slow and the action of the heart is weak. Prognosis in the greater majority of cases is unfavorable. The patients die within a few days. Pathologically, the process is a common edema of the skin, also involving the subcutaneous layer and the deeper tissues. Histologically, the skin does not correspond to that of a normally developed infant, but rather to the skin of a fetus of the sixth to the eighth month.

Earlier writers (Knofelmacher, Sanvorat, Mitchell, Theimich and Jaeckle [29]), analyzing the fat of scleremic infants, advance the theory that there is a loss of fluidity of the body fat and, because of the lowered temperature, sclerema results. Fat is composed of palmitic and stearic acids which solidify at a lower temperature. Oleic acid, which is the liquid fatty acid, is also a component of the fat. The fat of infants normally contains more of the solid fatty acids (palmitic and stearic). These writers believed that in sclerema the proportion of the solid fatty acid (palmitic and stearic) of the tissues was increased and, with the lowered temperature, brought about the hardened condition of the skin.

Smith [30] examined chemically the subcutaneous fat in an infant suffering from sclerema. He analyzed the fat from the normal areas of the skin, also the fat contained in the scleremic area of the infant's skin. He concluded that the subcutaneous fat taken from the scleremic

29. Quoted by Smith, C. S.: J. Cutan. Dis. **36**:436 (Sept.) 1918.
30. Smith, C. S.: Footnote 29.

area of the infant's skin had a higher fatty acid content than the subcutaneous fat taken from a normal area of the same infant's skin. There was no indication of any difference in the oleic acid content of the two fats. These findings do not justify a conclusion as to the etiology of sclerema. However, they seem to indicate that the change taking place in the subcutaneous fat is similar to a fat necrosis and not due to the absence of oleic acid.

Pernet [31] reports two cases of partial sclerema occurring in new-born infants. Although neither the clinical findings nor the Wassermann reaction sustained a diagnosis of syphilis as the causitive factor, mercury medication had a favorable effect on the condition, both infants recovering from the disease.

Bourne [32] treated an infant who had sclerema with thyroid extract, one-fourth grain daily, and, with the application of external heat, endeavored to combat the subnormal temperature. The infant improved rapidly during the first month, and, at 6 months of age, no evidence of sclerema remained.

SCLERODERMA

Scleroderma is divided into two main types: (1) the generalized or diffuse type, which may be associated with scleradactylia; (2) the localized or morphea type.

Goodman [33] describes an acute form of diffuse scleroderma occurring in a girl, 9 years old, following an attack of tonsillitis. The skin of the forehead, scalp, back of the neck and shoulders, as low as the spines of the scapulae, the cheeks, the chin and the neck as far down as the clavicles was most markedly affected. The eyelids drooped, appeared stiff and gave the child an inattentive and stupid expression. There were no wrinkles in the skin, which was warm and dry, felt thickened but inelastic and had a boardlike hardness. It was not possible to pinch up any skin between the thumb and forefinger. There was no pitting on pressure. The forehead could not be wrinkled, nor could the lower eyelids be retracted downward. The mouth could be opened only partly. The child was unable to whistle. Active and passive movements of the head, extension, flexion, lateral flexion and rotation were limited. During four weeks' stay in the hospital, the child failed to improve. She was given daily oil rubs. Thyroid extract in one-fourth grain doses daily was administered by mouth. She was then discharged from the hospital under the same treatment. Four months after her discharge, her appearance had changed considerably. She was

31. Pernet, G.: Brit. J. Child. Dis. **15**:218 (Aug.) 1918.
32. Bourne, E.: Lancet **1**:368 (Feb. 25) 1922.
33. Goodman, H.: Jour. Cutan. Dis. **6**:210 (April) 1918.

brighter. The skin of the scalp retained its hardness and immobility, but the eyelids and cheeks were soft and pliable and the hardness of the rest of the skin was gone.

Weidman [34] described a case of congenital scleroderma and sclerodactylia occurring in a new-born infant. The interesting factor in this case is the age of the child. Histologic study of the skin led Weidman to this diagnosis, as the microscopic picture clinically resembled that found in scleroderma of childhood and adult life.

Aronstam [35] reports a case of scleroderma in a girl, 15 years old. At 7 months, she fell and struck the right arm. At the time of the injury, no lesion was noticeable except a mild ecchymosis, which subsided in two weeks. Two months after the injury, a sclerotic patch appeared at the site of the trauma, which rapidly spread upward toward the middle third of the arm and downward to within 1 cm. of the metacarpus. Clinically, the lesions were waxy, yellowish brown, livid areas and bands longitudinally arranged along the extensor surface of the right arm. The skin was rigid and tightly bound down to the underlying structure. The cutaneous sensibility was normal.

Regarding the etilogy of scleroderma, Foerster [36] believes that there is reasonable evidence for attributing an important part in the etiology of scleroderma to morphologic and functional changes in the internal secretory organs, especially the thyroid gland. This newer idea would seek to displace the accepted view that scleroderma is an "angiotrophoneurosis."

The consensus of opinion today, in reference to the etiology of scleroderma, is that the affection is at least closely related to disturbances of function or "unbalance" of secretion of one or more of the ductless glands. Supporting this idea is the report of a case of scleroderma by Shamberg [37] occurring in a child who was a cretin.

A great many of the cases of scleroderma follow colds and exposure to wet and draughts. A history of preceding tonsillitis is given in many of the recorded cases.

Berrheim-Karrer [38] describes five cases of necrosis of the subcutaneous tissues in the new-born (so-called scleroderma of the newborn). A common feature of all his cases is the occurrence of infiltration in the deeper layers of the skin. The favorite sites are the back, outer surfaces of the arms, cheeks and chin. The size varies from that

34. Weidman, F. D.: Necropsy Findings in Case of Congenital Scleroderma and Sclerodactylia, Arch. Dermat. & Syph. **1**:375 (April) 1920.
35. Aronstam, N. E.: Urol. & Cutan. Rev. **26**:77 (Feb.) 1922.
36. Foerster, O. H.: J. Cutan. Dis. **34**:1 (Jan.) 1916.
37. Shamberg, J. F.: Tr. Am. Dermatol. Ass'n, June, 1919.
38. Berrheim-Karrer: Schweiz. med. Wchnschr. **52**:12 (Jan. 5) 1922

of a lentil to that of a plate. The author observed these nodes twice on the seventh day, once on the eighth day, once on the eleventh day and once on the thirteenth day after birth. The author never observed scar formation in contrast to atrophy in genuine scleroderma. Disappearance of the nodes occurred between the twenty-eighth and sixty-ninth day after birth. Microscopic examination proved the lesions to be in the subcutaneous fat. No bacteria could be found. The fatty tissue was strikingly rich in cells and network. The necrosis was limited to the individual fat cells. The characteristic structures of the fatty tissue were completely lost and some areas did not even reveal the presence of septums. This scleroderma of the new-born is a fatty necrosis of the subcutaneous fatty tissues. There is a marked clinical and histologic difference between the genuine scleroderma and this form.

Brinchmann [39] reports a case in a boy, 5 weeks old, who was born in a state of asphyxia. He had extensive thickening of the subcutaneous tissues, on the extremities, the thorax and the back. They were not prominent over the level of the skin. The temperature had always been normal, as well as the body functions. The subcutaneous prominences disappeared slowly, so that, after a period of five or six months, they were no longer visible. The histologic examination of a specimen of the skin disclosed amorphous masses in the subcutaneous fat lobules. There were no degenerative processes. The amorphous masses were formed of calcium as revealed by the silver nitrate coloration with Hubschmann's reagent and by the addition of hydrochloric acid. The author called this condition sclerema neonatorum. However, he remarks that it is not true sclerema, as is shown by the normal temperature, and the normal body functions, in addition to the fact that true sclerema is fatal. This case presented a condition somewhat similar to that reported by Berrheim-Karrer,[38] with skin manifestations clinically resembling scleroderma. Careful study, however, reveals that these cases present separate entities.

ACRODYNIA: ERYTHREDEMA, PINK DISEASE AND EPIDEMIC ERYTHEMA

Bilderback [40] described six children with a disease characterized by profuse sweating without odor, with swollen red feet and hands that are painfully sensitive to the touch. The hands and feet are cold and clammy, and the skin of the hands and feet are in the state of desquamation. The body, legs and arms may or may not have a rash. The rash is similar to an erythema or intertrigo that at times borders on an eczema and itches. Added to the local symptoms, there is a

39. Brinchmann, A.: Norsk. Mag. f. Lægevidensk. **83**:269 (April) 1922.
40. Bilderback, J. B.: Northwest M. J. **19**:263 (Oct.) 1920.

progressive loss of weight and marked weakness and apathy that at times approaches stupor. Bilderback [41] gave no specific name to this disease in his initial report.

Byfield,[42] in an excellent treatise, reported seventeen similar cases in children, all under 4 years of age. He remarks that the disease has a close resemblance to pellagra, but that so many manifestations argued against such a diagnosis that it was necessary to consider the possible presence of some other disease.

The clinical picture as given by Byfield is a complex one, the nervous system and the skin being the most involved. Respiratory and digestive tracts are less affected. In the nervous system, the changes are chiefly sensory or atrophic in character. Alopecia and pulling out of the hair occur in some cases. Falling out of the teeth, with only slight involvement of the gums, photophobia and, in one case, neurokeratitis were seen. Changes in the nails and reddening of the tongue also occur. Paresthesia of the toes and feet and of the fingers and hands was another constant and often most distressing symptom. The reflexes are diminished in almost all cases and absent or increased in some. Dullness and apathy, alternating with extreme restlessness and sleeplessness, were observed. In a characteristic case, the patient would often adopt an atypical posture, either lying on the side, rubbing the hands or feet, or crouching with the head buried in the pillow.

The skin manifestations are uniform. A symmetrical involvement of the fingers and toes, recurring at intervals of a fortnight or so, or even tending to be more or less constant, was one of the most striking characteristics of the disease. With the hands and feet cyanotic and cold, there appeared a non-confluent erythematous rash, most marked at the tips of the fingers and gradually diminishing until, at the region of the wrist, it had quite faded away. In some cases, a small number of fine papules rose from the area of erythema. Confluent erythema was the rule on the distal phalanges. Desquamation, most marked at the tips of the fingers and toes and growing less toward the region of the wrists and ankles, was often present. The feet were only slightly less involved than the hands. Never was there observed anything like a clean cut line of demarcation between affected and untouched skin as is seen in pellagra. When the thorax or approximate portions of the arms and legs showed skin manifestations, these consisted in either a morbilliform breaking-out or bullae, the latter being seen only in severe and more advanced cases.

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41. Dr. J. B. Bilderback of Portland, Ore., was the first author to describe acrodynia in this country. The description of his cases was sent by his associate, Dr. Patrick, to Dr. Weston of Charleston, S. C., who suggested the name acrodynia for this condition.

42. Byfield, A. H.: A Polyneuritic Syndrome Resembling Pellagra-Acrodynia (?) Seen in Very Young Children, Am. J. Dis. Child. **20**:347 (Nov.) 1920.

When an eruption appeared on the body, it was usually accompanied with paresthesia. When the eruption disappeared, pigmented spots were sometimes left. In two cases, the cheeks and the tip of the nose were involved. The nails are rarely involved.

An extreme and obstinate anorexia was the prominent feature of the disease. Failure to take a sufficient quantity of food would seem to be responsible for the marked degree of emaciation which is almost invariably present in these children who have been sick for several months. Many of the patients suffered extreme thirst. Unusual sweating was common in more advanced cases.

Frequency of urination was an almost uniform symptom. This was probably accompanied by distress, as many of the children continually complained of a desire to empty the bladder. Pyelitis was frequently present, though it was never extreme and readily yielded to treatment.

In a study of the diets of these children previous to development of the disease, no connection could be established between the previous diet and the onset of the disease.

A postmortem examination was made in one case, observed by Byfield. There were interesting changes present in the central nervous system. In the spinal cord, gliosis about the central canal was found. Some of the anterior horn cells proximal to the anterior commissure were found to be of poor staining quality. The sciatic nerve showed edema and swelling of the myelin sheath, as well as of the connective tissue about the nerve fibers. No cellular infiltration was observed. The same variation in the size of the fibers was seen in the posterior roots in the lumbar cord. Edema and swelling of the myelin sheath were also seen in the fibers of the dorsal root in that portion of the nerve lying between the ganglion and the spinal cord.

Since these original papers, numerous observers, Emerson,[43] Cartin,[44] Zahorsky,[45] Wood,[46] Weber,[47] Field,[48] McNeal,[49] Thursfield,[50] Davis,[51] Vipond,[52] Porter,[53] and Lindsay[54] have reported cases of

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43. Emerson, P. W., and Green, H.: Acrodynia, J. A. M. A. **77**:285 (July 23) 1921.
44. Cartin, H. J.: Pennsylvania M. J. **24**:287 (Feb.) 1921.
45. Zahorsky, J.: Mississippi M. A. J. **18**:153 (May) 1921; Semeiology of Pink Disease (Erythredema, Acrodynia), J. A. M. A. **79**:1975 (Dec. 9) 1922.
46. Wood, A. J.: M. J. Australia **1**:145 (Feb. 19) 1921; Am. J. Trop. Med. **1**:291 (Sept.) 1921.
47. Weber, F. P.: Brit. J. Dermat. & Syph. **33**:228 (June) 1921; **34**:111 (April) 1922.
48. Field, M. C.: Arch. Pediat. **39**:116 (Feb.) 1922.
49. McNeal, M. D.: Minnesota Med. **5**:153 (March) 1922.
50. Thursfield, H., and Paterson, D.: Brit. J. Child. Dis. **19**:27 (Jan.) 1922.
51. Davis, C. M.: Arch. Pediat. **39**:611 (Sept.) 1922.
52. Vipond, A. E.: Arch. Pediat. **39**:699 (Nov.) 1922.
53. Porter, L.: M. Clinics. N. America **6**:431 (Sept.) 1922.
54. Lindsay, L. M.: Canad. M. A. J. **12**:618 (Sept.) 1922.

acrodynia from various parts of the country and abroad, showing the wide distribution of the disease.

There is no specific treatment for acrodynia. A rational diet with hygienic measures gives the best therapeutic results.

PERLÈCHE

Perlèche is described by Smith,[55] also by Lane.[56] It is preeminently a disease of infancy and childhood. It is an affection of the labial commissures, almost always bilateral, and usually rather closely limited. As it progresses, the process extends for a varying distance toward the center of the lips, and usually extends a little way onto the skin surfaces and the true mucous membrane of the inner side of the lips. At the beginning of the disease, the epithelium is smooth and whitish, with a mother-of-pearl tinge. As it progresses, the epithelium becomes macerated and a little thickened, and loses most of the mother-of-pearl color. Small transverse fissures appear, which show a red base, if the lips are stretched, but do not reach the lower layers of the epidermis, and do not bleed easily even if rubbed. In some cases, there is slight erosion, but the surface is ordinarily not denuded. It is never an ulceration, and there is no swelling of the lips connected with it. There is little or no inflammatory area around the lesion. As the lesions begin to heal, their appearance approaches that of the early lesions, and after the roughness has disappeared, there remains only a slight discoloration, which persists for a month or so. No scars are left. If treated, the disease is usually cured in two or three weeks. If left to itself, there is usually spontaneous cure in a month or so, unless there is reinfection; but, in some cases, it is of indefinite duration.

In the mild cases of perlèche, there are no subjective symptoms at all. In the fully developed cases, there is a slight feeling of irritation, which causes the child to run the tongue over the lesion. It is probably from this sign that the disease develops its name (perlèche, meaning "licked"). There is never enough discomfort to cause the child to rub or pick the lesions. There are no other lesions or physical signs. There is never more than the slightest inflammatory reaction. The lymphatic glands are never enlarged.

Streptococcus plicatilis is probably the causative organism, although the disease has not been successfully reproduced in animals or human beings with this organism.

Auche[57] studied the histopathology of one case of perlèche and found cellular infiltration of the connective tissue of the papillae, dilata-

55. Smith, A. L.: Arch. Pediat. **34**:274 (April) 1917.
56. Lane, J. E.: Perlèche, J. A. M. A. **69**:192 (July 21) 1917.
57. Auche, quoted by Lane, J. E.: Footnote 56.

tion of the blood and lymphatic vessels, thickening of the interpapillary plugs, enlarged intercellular spaces in the prickle cell layer, with leukocytic infiltration, and in the upper part of this layer, serofibrinous infiltration and some intercellular cavities filled with polymorphonuclear leukocytes. Some of the prickle cells were degenerated, opaque and without nuclei.

Perlèche is highly contagious. Common drinking utensils are the most frequent vehicles of transmission. Other ways in which it is spread is by kissing and the use of common pencils, handkerchiefs and towels.

The treatment is simple. Prompt cure is affected by painting the lesions daily or every other day with a 10 per cent. solution of silver nitrate or a diluted tincture of iodin.

CUTANEOUS TUBERCULOSIS

Wise and Satenstein [58] describe the clinical and histologic feature of papular necrotic tuberculids, together with the presentation of two cases occurring in children. They mention the occurrence of folliclis, acinitis and lupus erythematous in association with the papulonecrotic tuberculids, which are relatively common. It is conceded by the majority of the prominent workers in the field of dermatology that folliclis and acnitis are two more or less similar clinical manifestations of one or the same dermatosis. Folliclis is the more superficial form. It appears as necrotic papules, most frequently on the back of the fingers and hands; on the palms at times; on the ulnar surface of the forearms, and about the points of the elbows. It often attacks the skin of the trunk and the lower extremities.

Acnitis is the deeper form, the necrotic papules affecting chiefly the face. The eruption on the hands is frequently associated with periones of the fingers, or merely the acro-asphyxia and an eruption of facial lupus erythematous. Among the modern writers, there is a growing tendency to regard folliclis and acnitis as so closely related nosologically that the same interpretation of the pathogenesis is applicable to both types of eruption. While there seems to be a practically unanimous agreement as to the tuberbacillary nature of folliclis, the same unanimity of opinion does not obtain with regard to acnitis. The consensus of opinion is that, while folliclis is always a tuberculous disease, acnitis may be at times a tuberculous manifestation, at other times non-tuberculous, very much as is, presumably, the case with lupus erythematous. The clinical observer cannot ignore the patent fact that a majority of patients presenting the papulonecrotic lesions of folliclis on the upper extremity have also a papulonecrotic eruption on the face.

58. Wise, F., and Satenstein, D. L.: Clinical and Histologic Features of Certain Types of Cutaneous Tuberculosis, Arch. Dermat. & Syph. **4**:586 (Oct.) 1921.

The pathogenesis of the papular necrotic tuberculids and the associated conditions—folliclis, acnitis and lupus erythematous—has caused spirited controversy. The pathogenesis of these eruptions is still a partly unsolved problem. The tuberculids have been defined as "local reactions wherein nature has set up a cutaneous reaction, which indicates the response of the skin to the products (or derivatives) of tubercle bacilli." Zieler [59] regards them as "reactions of cutaneous hypersusceptibility in tuberculous individuals, provoked by disseminated tubercle bacilli, these reactions as a rule leading to the destruction of metastasizing tubercle bacilli." The modern conception postulates the existence of a hematogenous tuberculous infection. It is presumed that the lesions result from the activity of isolated tubercle bacilli, occurring in scant numbers in the skin. The bacilli circulating in the blood stream ultimately find a resting place in the blood vessels of the cutis, there to be subjected to the action of the various antibodies, finally undergoing lysis, and liberating certain toxins, which presumably play a part in the formation of the papulonecrotic lesions.

The histopathologic study of acnitis and folliclis reveals few very typical changes, whether the tissue is obtained from fresh or from old papules. Most of the sections show merely the ordinary alterations which characterize inflammatory tissue; namely, cell infiltration, consisting of numerous round cells and few plasma cells. These infiltrates, occurring frequently about the sebaceous and sweat glands, undergo a slow process of necrosis. Involution takes place after spontaneous extrusion of the broken down mass. The lesion heals, leaving a deep, sharply defined round scar, often surrounded by a zone of pigmentation. On the other hand, the presence of epithelioids and giant cells has been observed by several investigators. Briefly stated, it may be said of the papulonecrotic tuberculids that, in the present state of our knowledge, the clinical diagnosis has far more weight than the histologic.

According to Lewandowsky,[60] the simplest histologic change in the papulonecrotic tuberculids, as is the case in all other hematogenous tuberculosis of the skin, consists of a circumscribed infiltrate of tuberculoid structure in the cutis. Often the microscopic appearances present little or no evidences of a tuberculous structure, the usual findings being those corresponding to an ordinary reaction in the skin. But those investigators who have had the opportunity to examine a large number of sections, obtained from various types of lesions, have on numerous

59. Zieler: Die Tuberkulose der Haut, in Jesionek's Haut und Geschlechts-Krankheiten, 1914, quoted by Wise: Footnote 58.

60. Lewandowsky: Die Tuberkulose der Haut, Enzyklopaedie der klinischen Medizen, Berlin, 1916, quoted by Wise: Footnote 58.

occasions demonstrated in the cutis many small areas containing large giant cells, together with collections of epithelioid cells, so suggestive of tuberculosis. The most characteristic feature, however, is the necrosis. Small areas of necrosis may occur in any portion of the cutis, the surrounding tissue exhibiting a narrow band of epithelioid cells and lymphocytes. Such areas of necrosis are often observed in the upper portion of the corium, just beneath the epithelium, the latter taking part in the destructive process. On either side of the necrotic area, the epithelium shows evidences of proliferation, with edema, hyperkeratosis, and parakeratosis of the epidermis.

The first case presented was that of a girl of 13 years. She had the characteristic patch of lupus erythematosus over the dorsum of the nose. The color of the lesion varied through all shades of inflammatory red. There were fine scales, grayish to grayish yellow, rather scant, and most pronounced over the border. On the cheeks, in the shape of the wings of a butterfly, were numerous small necrotic papules, the so-called "acnitis." The lesions were dull red, resembling the papules seen in variola, and having a necrotic center. There were also some small soft scars present. The scars did not seem to have the tendency to contract and cause disfiguration. Over the dorsum of the fingers were several similar lesions, typical "folliclis." The child appeared healthy otherwise. There was no other evidence of tuberculosis on physical examination. The second case, in a boy, 11 years old, who had many necrotic papules over the anterior surface of the thighs and legs, presented papules, most numerous in the region of the knees, sharply defined, dark red, and having necrotic centers. There was no scarring present at this examination. The rest of the cutaneous surface was free from lesion. These were frank papulonecrotic tuberculids.

Wise and Satenstein [50] state that the appearance of tuberculids in infants and young children points to the existence of visceral tuberculosis, and is therefore of grave significance, especially since the cutaneous eruption is often the first manifestation of the infection and hence may be a valuable warning signal. The concomitance of cutaneous tuberculids and phthisis, tuberculous adenitis and other manifestations of visceral or bone tuberculosis is quite common. Sales [61] reports a case of papulonecrotic tuberculids in a child, aged 2 years. The necrotic papules were followed by fatal miliary tuberculosis. Inoculation of guinea-pigs with tissue consisting of the necrotic papules produced tuberculosis in the guinea-pigs.

Stokes [62] remarks that he has been fortunate in securing fairly successful results by the use of arsphenamin in the treatment of papulonecrotic tuberculids. The technic and dosage are essentially the same as those employed in the treatment of syphilis. The effect is nonspecific and consists in an elevation of the general resistance of the patient rather than in any parasiticidal action on the tubercle bacilli.

61. Sales, G.: Arch. de méd. d. enf. **25**:513 (Sept.) 1922.
62. Stokes, J. H.: Northwestern Med. **20**:79 (April) 1921.

Cowie[63] reports a case of granuloma rubra nasi—tuberculosis cutis—occurring in a boy, 4 years old. The boy was markedly underweight and had never made the normal average gain in weight even as an infant. He was brought to the hospital on account of redness of the nose, developing in early infancy and persisting ever since. The child presented, over the chest, arms and abdomen, an eruption which consisted of small dusky red papules. There was no weeping at any point. There was no eruption over the face similar to that seen on the body. The eruption or process on the nose was quite different. The entire nose was red, the redness being accentuated at the tip. On close examination, there were many small papules which, when pressed with a glass slide, showed minute yellowish brown points, the so-called apple jelly nodules of cutaneous tuberculosis. The hands and wrists were red, beginning at the tips of the fingers. The redness continued up to the middle of the forearm. There were no abrasions of the finger tips. The child did not put the fingers in the mouth, nor did he seem to exhibit any evidence of pain in the fingers or toes.

The absence of paresthesia was an important differential point in ruling out acrodynia as a diagnosis in this case. An interesting feature of the case was the absence of a positive cutaneous tuberculin reaction. However, this is not unusual, as the marked degree of undernourishment would explain the absence of a positive test.

Sillians[64] presented a Polish boy of 10 years, who had tuberculosis verrucosa cutis, lupus vulgaris and lichen scrofulosorum. The lesion appeared on the foot shortly after birth and spread upward, taking the form of a raised warty looking mass and papillary projections, mostly crusty, with no ulceration or moisture. Roentgen-ray treatment made the lesions tender and moist. Further reaction caused an itching eruption on the body (lichen scrofulosus).

All this is symptomatic of a group of tuberculous skin lesions. Tubercle bacilli of attenuated virulence have been found in tuberculosis cutis and lupus vulgaris. Reactions to tuberculin have produced lichen scrofulosus, as the roentgen ray did in this case. The Pirquet reaction is negative because of the formation of antibodies. There was no scarring in this patient; but the prognosis for recovery is only fair. Treatment consists of judicious use of the roentgen ray.

ICHTHYOSIS

Thibierge and Legrain[65] present three cases of fetal ichthyosis. The disease was first manifested at birth or within the first few months of life. Other congenital malformations have been met in conjunction with the ichthyosis. The hyperkeratosis seen in these cases seemed peculiar to each of the body regions. There was an associated seborrhoea of the hairy scalp in one case. Erythoderma was observed in one case of the series. Fetal ichthyosis constitutes a very precise pathologic type. The cause of the affection remains obscure. The

63. Cowie, D. M.: M. Clinics N. America **6**:1301 (March) 1923.
64. Sillians, A. W.: Internat. Clinics **2**:32, Series 31, 1921.
65. Thibierge, G., and Legrain P.: Ann. de dermat. et syph. **2**:337 (Aug.) 1921.

fact that syphilis may be a concomitant disease does not render it any easier to determine whether or not syphilis is an etiologic factor.

Jordan [66] observed two cases, one of which was true ichthyosis congenita. The other, which the author considered a milder type of ichthyosis congenita, and which was designated ichthyosis larvata, appeared at first to be ichthyosis congenita. However, under treatment, the skin softened, and after all of the cutaneous phenomena disappeared, the condition resembled ichthyosis larvata. The histologic picture of both conditions is similar: hypertrophy of the superficial epithelium and excessive development of the sweat glands. In ichthyosis larvata, the changes are of a milder type. DeStefano [67] reports a case of congenital ichthyosis in an infant who is now 3 months of age. He believes the condition to be of syphilitic origin, as both the father's and mother's blood gave markedly positive reactions. Henrichsen [68] also reports a case of congenital ichthyosis in a child who died at birth. The entire body was affected so that the body functions were markedly altered.

McGlasson [69] presents two cases of onychogryposis hysterix and keratosis follicularis, occurring in two brothers, aged 17 and 11 years. Except that they were both undersized, physical examination was negative. They were well developed sexually. The clawlike nails of the fingers and toes varied from 2 to 5 cm. in thickness, the degree of deformity corresponding to the proportionate size of the nails on the different toes. The deformity interfered with walking or wearing shoes. Ichthyosis was most marked on the flexure surface of the arms, around the neck and over the abdomen. Keratosis follicularis was more evident on the extensor surface of the arms and legs and in the scapular region. The Wassermann reaction was negative. The older boy was of the moron type. The younger boy was very bright. Surgical extirpation was performed in each case. In the older boy, the nails regained their former condition; in the younger, there was 50 per cent. improvement in new nails. The better method of treatment is the employment of actual cautery to destroy the matrix. The body lesions responded best to applications of boric acid and white petrolatum. This loosens the skin and softens the horny plugs so that they come away easily. As the condition is congenital, treatment must be continued indefinitely.

Mackee and Rosen [70] gave a description of the clinical picture of erythodermia congénitale ichthyosiforme, and presented a child, 14 years old, who had this condition.

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66. Jordan, A.: Dermat. Wchnschr. **74**:585 (June 24) 1922.
67. DeStefano, O. S.: Pediatria **30**:672 (July 15) 1922.
68. Henrichsen, J.: Ugesk. f. Læger **84**:1277 (Sept. 28) 1922.
69. McGlasson, I. L.: Texas State J. Med. **17**:255 (Sept.) 1921.
70. Mackee, G. M., and Rosen, I. R.: J. Cutan. Dis. **35**:235 (April) 1917.

The condition is present at birth in the majority of the cases or develops shortly afterward. Heredity does not appear to play an important rôle. It is about equally common in the two sexes. As a rule, the disease begins with a more or less generalized erythrodermia, which may be marked or inconspicuous. A thickening of the horny layer may precede the erythema. As the patient grows older, the reddened area becomes thickened and scaly, while the erythrodermia is likely to fade gradually and may disappear entirely in adult life. The ichthyotic skin remains, although it too may undergo some improvement. The face is usually red and slightly scaly. Ectropion may be present. The scalp is usually seborrheic.

There are two general types of the affection; namely, the dry type and the bullous type. The former has already been outlined. The same description will answer for the bullous type, with the exception that there are outbreaks of the bullous lesions. The bullae occur most frequently on the extremities. They are very flaccid and disappear without producing scars.

The disease is usually generalized and symmetrical. Cases have been described, however, in which there are circumscribed, symmetrical lesions. In some instances, the lesions are sharply marginated. In others, the margins are not closely defined. Perspiration does not occur over the general cutaneous surfaces, but there may be hyperhidrosis of the palms and soles. The general health is unimpaired, and there are no objective symptoms, with the exception of more or less pruritis in some of the cases.

An erythrodermia congénitale ichthyosiforme seen in a 14-year-old girl was first noticed at 5 months, when red areas developed here and there over the body. A few months after the onset of the erythema, the lesions became scaly. Later, the thickening of the skin was a marked feature, so that by the fifth year the affected areas of the skin were thickened and dark brown or black in color. The eruption occurred in remissions, the skin improving during the summer months. The etiology of this condition is obscure. Nothing is offered in the form of treatment.

MISCELLANEOUS DISEASES

Weber [71] describes a child, aged 4, with a congenital hypertrichosis or hirsutes. The hypertrichosis affected the forehead, temples, sides of the face, the back and the upper and lower extremities. The regions of the groins, pubes, front of the trunk and the neighborhood of the mouth and nose are not hairy. There was nothing to suggest the presence of a hypernephromatous tumor in the abdomen, and a roentgenogram of the base of the skull showed nothing abnormal about the

71. Weber, F. P.: Brit. J. Child. Dis. **14**:272 (Oct.) 1917.

pituitary fossa. There is no sign of any precocious or abnormal sexual condition. There was no evidence of congenital syphilis. The Wassermann test was negative.

Weber [71] mentions two types of hypertrichosis, the first of which is termed the "simian type," in which the hypertrichosis is congenital or developmental and sometimes familial and is regarded as an example of the so-called "degenerative reversion." The second type is associated with, and secondary to, disorders of the endocrine organs.

Hutchinson [72] presented an infant, 4½ months old, having numerous nodules scattered over the face, head, ears, body and legs and one on the palm of the right hand. The nodules were situated in the skin and varied in size from a pinhead to a 5-cent piece. They also varied in color from light yellow to brown. There was no tendency to breaking down. The physical, blood and serologic examinations were negative. A nodule was studied by microscopic examination, and Hutchinson concluded that these tumors were multiple primary carcinoid of the skin.

Blaisdell [73] reports a case of congenital alopecia in a child of 4 years. The boy's history, familial and personal, showed nothing of interest. The physical examination was negative. Owing to the baldness, the boy had the appearance of an elfish old man, so characteristic of those without hair either on the scalp or on the face. The hair on the scalp was extremely scanty, consisting of thin straight shafts about one-half inch (1.3 cm.) apart and 1 inch (2.5 cm.) long. The scalp itself appeared to be decidedly parchment-like owing to the lack of subcutaneous fat. The eyebrows were represented by from six to ten small lanugo hairs. The interesting feature of the boy's skin was the asbolute lack of any hair follicles and the extreme dryness of the skin, as the result of the deficiency in the sebaceous and sweat glands. The child suffered no objective symptoms. The important and striking features of the case, based on a careful microscopic study of ten serial sections from different parts of the skin, was the comparatively few blood vessels. Only one erector pili muscle was seen. There were no hair shafts and no sebaceous or sweat glands.

Smith [74] observed a girl, aged 8, with an extensive pigmented and hairy nevus associated with molluscous tumors. At birth, the face, trunk and limbs were covered with dark reddish brown marks, which had since grown in proportion to the growth of the child. At the present examination, almost the whole of the cutaneous surface was covered with pigmented patches, varying in color from reddish to

72. Hutchinson, W.: J. Cutan. Dis. **31**:161 (Feb.) 1913.
73. Blaisdell, J. H.: Boston M. & S. J. **176**:210 (Feb. 8) 1917.
74. Smith, W. M.: Brit. J. Child. Dis. **12**:299 (Sept.) 1915.

blackish brown. Some of the patches were covered with long and abundant hair, while others were smoother and showed shorter hair.

The skin of the back, especially along the spine, showed a dark pigmentation and was covered with long coarse hair. The skin of the left leg was also dark and hairy, both front and back. In the unaffected areas, which are chiefly seen on the forearm and back of the right leg, the skin was in excellent condition.

On the left arm and leg, which were thinner than the right, the lesions were more pronounced than on the opposite side. The left arm was wasted, and here the whole of the skin was diseased and resembled a monkey's skin in texture.

In addition to the nevi, the child presented a number of molluscous tumors. The largest, which was about 4 inches (10 cm.) long, was attached to the inner side of the left buttock and perineum on the left side. This tumor was divided into two lobes by a fissure midway along the perineum. There was a second tumor, external and inferior to the larger one, in the midline of the left buttock.

Apart from the skin condition and the difference in the size of the limbs on the two sides, the child presented no abnormalities.

The presence of the pigmented and hairy nevus is not uncommon. A similar condition was reported by Fox [75] in 1912.

Nass [76] describes a case of keratoma palmare and plantare hereditarium in a boy, aged 14 years, which developed on the fingers when the patient was 3 months old. At the time of the present examination, it involved both the hands and feet. The affection consisted of thickening of the horny epidermis which formed plates from the thickness of a finger nail to an eighth of an inch or more. The finer markings on the palms and soles were obliterated, while the coarser markings were deepened. The borders of the plates were sharply defined and without inflammatory areola. This is a rare disease. An interesting feature in this case is that there was an area on both forearms about 3 fingers wide of extra sensibility to pain and to the faradic current. The central nervous system presented nothing noteworthy. The lesions themselves were hyperalgesic. The histologic picture showed, in addition to the marked increase of the horny layer of the skin, the presence of streptococci, a feature that had never been noticed before.

Borghoff [77] describes a case of Darier's disease, an unusual skin manifestation characterized by the occurrence of a follicular keratosis, with a peculiar histologic picture. Borghoff gives a description of the

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75. Fox, Howard: A Case of Extensive Pigmented and Hairy Nevus, J. A. M. A. **58**:1190 (April 20) 1912.
76. Nass, H.: Dermat. Ztschr. **33**:338 (July) 1921.
77. Borghoff, J. A.: Darier's Disease in Infant, Arch. Dermat. & Syph. **4**:609 (Oct.) 1921.

first case in which the onset occurred in an infant, who, at the age of 4 months, presented an eruption over the upper portion of the back. This spread slowly in all directions and within three weeks had reached the size of the palm. About this time a similar eruption appeared on the anterior surface of the chest, and this also spread slowly. In three weeks, the condition had become rather widespread, involving the greater part of the back, chest and abdomen, the scalp being also affected at this time. Simultaneously with the appearance of the eruption, the child became extremely fretful during the act of defecation, at times refusing to move the bowels.

On examination, the anus was found to be involved in the general eruption. Over occiput and symmetrically over both temporal regions were many discrete, follicular, pinhead sized papular lesions of a yellowish brown, the majority of which were covered with a dirty brown or black greasy scale. These scales were particularly in evidence over the occiput. On removal of the scale, it was seen to consist of a thick horny plug which extended into the follicle, the papule being left with a minute funnel shaped depression in the center. Though discrete, the individual papules were rather closely aggregated, the scale formation over several of the papules giving the eruption a confluent appearance. A similar condition existed over the entire back and anterior surface of the chest, extending onto the abdomen and into the lumbar region. The lesions over the back and abdomen stood out as more characteristic papules than did those of the scalp. In the axilla and inguinal regions were a number of lesions which had become ulcerated as the result of the moisture and friction. The pruritis at times was intense, preventing the child from sleeping. On the hard palate, 0.5 cm. within the margins of the teeth, were a number of white papular lesions, firm to pressure and the size of a wheat seed. Those posteriorly were ulcerated and covered with a gray membrane, resembling the moist papules of a syphilid. They were symmetrical in their distribution and painful on manipulation.

At the mucocutaneous border of the anus, there was a distinct circular formation of papular efflorescences, each papule of an oval shape and the size of a wheat grain. They were arranged end to end, and were yellowish red, slightly infiltrated and very tender to the touch, causing much pain on defecation. Two of the lesions had become vegetative and presented an ulcerated flat surface.

The skin tissue, showing the more characteristic types of follicular papules, was excised from the scapular region and abdomen. The epidermis presented many changes from the normal. The horny layer was most involved, presenting a marked hypertrophy and a parakeratosis. In that portion nearest the rete were numerous cells which

had retained their nuclei, the latter being larger in many instances than those of the prickle cells. The condition was treated by the roentgen-ray therapy. This form of treatment is only palliative. The disease improved for a while; but finally the lesions became ulcerated, secondary infection set in and the child died. The cause of death could not be ascertained.

Abt [78] reports a case of congenital skin defect in a new-born infant who presented a defective skin area over each knee, 1 by 1¼ inches (2.5 by 3.1 cm.). They were symmetrical; that is, they were almost identical in size and shape, and seemed to be irregularly punched out. The skin around the edges was drawn and puckered, presenting the appearance of ulcers with irregular borders. The base was beefy red and moist. From week to week, the ulcers gradually covered over so that, after five or six weeks, the denuded red areas were replaced by shiny, white patches, somewhat lighter in color than the surrounding skin. The healing process was complete, and the baby seemed well in every respect.

The congenital skin defects are attributed either to errors in development or to inflammatory adhesions between the external layers of the skin and the amnion. At the point where this adhesion has taken place, the growth of flat epithelium is retarded. As the liquor amnii accumulates, the so-called Simonart's threads are formed. These are adhesions that form threads or bands between the amnion and the fetus. If these bands are torn loose from the integument of the fetus, a skin defect remains. Not infrequently, these skin defects are associated with other congenital malformations; for instance, deformities of the extremities, such as deficient fingers, hands or feet.

Bazel [79] reports a case of aplasia cutis congenita in one full-term twin, the other being a fetus papyraceus. The time of death of the fetus was estimated at about 4 months. It had its own amnion and chorion. The full-term twin, a boy, had a skin defect to the left and right of the navel, almost symmetrical, of the shape of a long rhombus, and reaching nearly to the posterior axillary line. The edge was formed of a whitish scarred stripe about 1 cm. wide. The rest of the surface was covered by a thin glistening skin which could not be removed. A granulating ulcer about as large as a penny was found in the center of the left side without epithelium. The healing ran a normal course, the ulcer being covered with epithelium on the fifth day after birth, and the red skin being considerably paler. The child was discharged as cured on the eleventh day.

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78. Abt, I. A.: Congenital Skin Defects, Am. J. Dis. Child. **14**:113 (Aug.) 1917.

79. Bazel, J.: Casop. Lek. cesk., Prague **61**:499 (June 3) 1922.

Shelmire [80] describes five cases of adenoma sebaceum occurring in one family, affecting the father, and four children, aged 12, 10, 6 and 3 years. The lesions arise chiefly from hypertrophy of the sebaceous glands. They vary from pinhead to pea size and are symmetrically distributed over the face. While many of the lesions are of the normal color of the skin, some are deep purple. The histologic picture of adenoma sebaceum shows that the sebaceous glands are increased in number and size and extend deeply into the corium. Some of the glands show cystic dilatation.

Josselyn [81] reports a rare skin disease in a child, 2½ years old, who presented brown round and oval areas irregularly scattered over the thorax, abdomen and back. The more exposed surfaces, such as the limbs and face, were not involved. The lesions, which were at first raised and looked like bee stings, gradually became flatter, and brown. The child was apparently in good health. The age of the patient; the mode of onset, chronicity and location, and the formation of wheals on rubbing were evidence in favor of urticaria pigmentosa. A condition closely resembling this one results from phenolphthalein poisoning, chronic, following long use of laxative phenolphthalein preparations. In this disease, the distribution is more general, the spots are yellow brown and no wheals are present. Treatment of urticaria pigmentosa is said to be of no use, the disease terminating at about the age of puberty. The usual treatment for urticaria may be tried.

Sibley [82] presented a girl of 5 years having monilethrix, the only one in her family affected. At birth, she had dark brown hair which was normal in appearance. At 1 month of age, the hair came out, and it had never grown properly since. It now had the appearance of flaxen tow, being from 1 to 2 inches (2.5 to 5 cm.) long on the vertex of the scalp, but only about one-eighth to one-fourth inch (0.3 to 0.6 cm.) in length over the occipital and parietal regions and the margin of the frontal region. The hairs were very brittle. The structural appearance of the eyelashes did not suggest monilethrix. The whole scalp presented the appearance of keratosis pilaris.

Golay [83] observed a girl with monilethrix for five years. The patient was born at full term. It was noticed that the scalp was dry and rough, and no hair could be seen on it. Rudimentary hairs began to appear toward the fifth month. The child is now 5 years old and shows a marked condition of keratosis pilaris. The hairs are dry, short

80. Shelmire, J. B.: Adenoma Sebaceum, J. A. M. A. **71**:963 (Sept. 21) 1918.
81. Josselyn, R. B.: J. Maine M. A. **12**:53 (Sept.) 1921.
82. Sibley, W. K.: Proc. Roy. Soc. Med., London **14**:70 (June) 1921.
83. Golay, J.: Ann. de dermat. et syph. **3**:294 (June) 1922.

and brittle and have the beaded appearance which is characteristic of monilethrix. The eyebrows, eyelashes and hairs of the body are affected. The Wassermann reaction is negative. Thyroid extract alone or associated with other glandular extracts produces no improvement.

Ferreira [84] studied the incidence of mongolian spots in 485 infants. The races represented were the white and the black (mulatto and negro). Mongolian spots were borne by 5 per cent. of the whites, 63 per cent. of the mulattoes and 43 per cent. of the negroes. The sacral region and buttocks were the sites of selection. The spots rarely occurred elsewhere. They were usually single, rarely multiple. One case presenting eleven spots was observed.

Eyzaguirre [85] observed mongolian spots occurring in Peru. The modern coast dwellers of Peru are of mixed stock; while the people of the Andes represent the pure Peruvian stock. The blue mongolian spots are borne by 80 per cent. of the native children of both stocks, but they are rarely found where the white blood predominates. The spots occur more frequently in boys than in girls, and the younger the child the more distinct the spot is. The pigmentation does not remain longer than four years and often occupies the sacrococcygeal area, which is the area most notably pigmented in mammals. Histologically, large cells appear in the dermis, bearing melanin or chromatoblasts. The spots are hereditary and are transmitted according to the mendelian law. They are characteristic of the Indian and the Mongolian races, the incidence being 72.48 per cent. Boisserie-Lacroix [86] made similar observations on the occurrence of mongolian spots in 1,000 children in Bourdeaux.

Halez [87] makes some interesting remarks on the desquamative dermatosis of the skin. Erythema of the skin, with more or less desquamation, is not rare in young infants. It is often epidemic among nurslings, beginning as a redness about the mouth. The erythema gradually spreads all over the body and vesicles or bullae develop. Sometimes the mucous membranes are affected. The vesicles finally dry up and the skin desquamates in large flakes. Death occurs in about half the cases in from eight to fifteen days. The affection seems to be primary and is not preceded by seborrhea of the scalp, by intertrigo or by gluteal erythema. Staphylococci and an unidentified diplococcus are found in the vesicular liquid and sometimes in the blood. The appearance is similar to that of phemphigus.

The treatment of infantile desquamative erythemas is hygienic rather than medicinal. Cleanliness is important. Soiled diapers should be

84. Ferreira, C.: Arch. de méd. d. enf. **25**:23 (Jan.) 1922.
85. Eyzaguirre, R.: Arch. de méd. d. enf. **25**:19 (Jan.) 1922.
86. Boisserie-Lacroix: J. de méd. de Bordeaux **94**:355 (June 10) 1922.
87. Halez, G.: Nourrisson **10**:6 (Jan.) 1922.

promptly changed. Bathing should be generally avoided, as it tends to irritate the skin. The infant may be bathed with a mixture composed of iodin, 1 gm., potassium iodid, 2 gm., and distilled water, 1 liter. The skin should be dried without rubbing and talcum dusted on.

Van Lohuizen [88] presented a new-born child with telangiectasia cutis and subcutis. These rare cutaneous changes are divided into two groups: (1) marble-like (veined) areas and (2) blue-red patches. The marble-like portions resembled the cutis marmorata of healthy nurslings, except that the phenomenon was more marked, the white patches between the meshes were larger and the limiting lines of the meshes were broader. The blue-red patches looked at first sight like vascular nevi. Their outlines were irregular, and the patches were not prominent over the skin. The skin presented prominent veins and also some small defects. The nose, lips, genital organs, ears, the volar surfaces of the hands and the plantar aspect of the feet were free from changes. The skin changes had persisted and existed for eighteen months after birth, but they were less marked.

The histologic examination of a speciman revealed a large number of vessels in the cutaneous and subcutaneous tissues. They were enlarged; but there was no other anomaly. The diagnosis, therefore, must be cutis marmorata telangiectasia congenita. The Pirquet and Wassermann reactions were negative. The nevi cannot be considered tumors. The most plausible hypothesis is that the skin anomaly was a developmental disturbance.

For many years, Lehnroff and Leiner [89] have noted an erythema occurring in children with endocarditis, with or without rheumatism. The disease is known as erythema annulare, a typical exanthem in endocarditis. This erythema is always of the same character and has probably been overlooked because of its delicacy and faintness. The erythema is so typical and constant that on it alone may be based the diagnosis of endocarditis. It appears at all ages in which joint diseases are seen but has not been observed in infancy.

The erythema does not appear at the onset of the rheumatism, but often develops after defervescence when the pallor and weakness lead to the suspicion of heart disease. Distinct endocarditis or suspicious cardiac murmurs were always found at the time of the eruption, the latter being the first sign of the disease in one case. The eruption is never seen in malignant endocarditis or endocarditis due to other infectious diseases (gonorrhoea, scarlatina, syphilis or sepsis).

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88. Van Lohuizen, C. H. J.: Nederl. Tijdschr. v. Geneesk. **66**:1259 (April 1) 1922.

89. Lehnroff, H., and Leiner, C.: Ztschr. f. Kinderh. **32**:46 (March 15) 1922.

The polymorphous exanthems described in rheumatism and endocarditis are never found simultaneously with erythema annulare. The latter is usually accompanied by other symptoms. The first efflorescences are small (1-3 mm.) rings of delicate rose, bluish or pale livid, few in number, over the trunk, especially the breast, upper half of the abdomen, the lateral part of the thorax and the back. The rings become more distinct if the child is uncovered for a time. They increase in size in a few days or hours, become confluent and form polycyclic figures. More rarely, they involve the extremities; most frequently the inner surfaces of the thigh, rarely the extensor surfaces. The face and mucosa are free. Edema, follicular hypertrophy, hemorrhages and itching are not observed, nor are scaling or pigmentation, after the eruption disappears. The eruption lasts only a few days and varies in distinctness. The intensity of the eruption bears no relation to the degree of the rheumatic process. Drugs can be definitely excluded in the etiology. Cultures from the blood and spots were negative. The absence of pustules with hemorrhages or necrosis argues against a metastatic bacterial focus.

Zurhelle [90] presented a boy, 13 years old, who showed the typical picture of parapsoriasis guttata with an extensive leukoderma. The individual efflorescences were brownish and covered by a firmly adherent lid-shaped scale. On lifting off the scale, there were no papillary hemorrhages such as are found in true psoriasis. The efflorescences were scattered over the whole back. The head was free, but the upper lids showed a few scales. There was also a marked leukoderma of the umbilicus and of the breast, extending to the stomach region and between the shoulder blades. The Wassermann reaction was negative. Spirochetes were absent and there were no other signs of syphilis.

With roentgen-ray treatment and the use of a salicylate salve, the efflorescences disappeared, but the leukoderma persisted. The case is noteworthy on account of the leukoderma and the localization of the efflorescences on the upper lids.

Gonella [91] studied skin pigmentation in thirty-three children and ten fetuses. Small specimens of skin were excised. This was generally carried out postmortem, but in a few cases a small amount of epidermis was removed in the living child. It was taken from the same region in all cases. The ages of the children varied from 8 months to 5 years. The youngest of the fetuses was 10 cm. long, the oldest was full-term. The specimens were hardened in formaldehyd. Sections were made with a microtome and were then treated with the dopa stain (dioxyphenylalanin), some with silver nitrate for four or

90. Zurhelle, E.: Dermat. Ztschr. **35**:338 (March) 1922.
91. Gonella, M.: Jahrb. f. Kinderh. **48**:123 (May) 1922.

five hours, without incubation. The reactions were on the average weaker than those for adults. A coherent line of pigmentation was found only in those children who had been cured of measles by means of irradiation or who had syphilitic exanthems and a particularly richly pigmented epidermis.

There was some pigmentation in all the skin specimens of the children. The fetuses presented various degrees of development of the epidermis, according to the age. Differences were also found between the still-born fetuses and those that had lived even for a short time. The pigmentation appears, therefore, to have some relation to extrauterine life.

Schmidt [92] reports cases of four children of the same family with xanthoma. The condition developed in early life. The disease was most extensive in the eldest child. None of the children showed evidence of organic disease. The liver was normal. There was an increased cholestrin content of the blood in all of the patients. As the disease occurred before puberty, and as all the members of the family were affected, the author considers the condition as xanthoma juvenile familiare hereditarium. Very little is known as to the duration of hereditary xanthoma. It seems that hereditary xanthomatosis lasts throughout the patient's life without material changes in its extent or in the size of the individual lesions.

Junes and Buckwell [93] describe a case of xeroderma pigmentosum in a boy, aged 7 years, the exposed parts of whose body were covered with patches of lentigo. On the face and neck, there were red vascular macules, nevis sclerotic and atrophic areas, and subcutaneous nodules, which gave rise to ulceration. Keratotic formations were present about the left ear. The right cornea and conjunctiva were infiltrated and vision was reduced. A tumor was attached by a pedicle to the external quadrant of the left cornea. The anterior chamber was obliterated and the iris adherent to the posterior surface of the cornea. The tumor was removed and roentgen-ray treatment was instituted. Soft rays were employed, the intensity being 1 milliampere and the duration of exposure ten minutes.

Bechet [94] presented a boy of 13 years who had pityriasis rubra pilaris associated with dystrophia adiposogenitalis. The boy gave a history of a fall from a subway platform with a resulting burn from the third rail, involving the right scapular region. One month after the accident, the eruption appeared, first in scaly patches, which subsequently became keratotic. Later, the palms and soles became hyperkeratotic. The patient was undersized, with marked obesity. The

92. Schmidt, E.: Arch. f. Dermat. u. Syph. **140**:408 (June 10) 1923.
93. Junes, E., and Buckwell, P.: Rev. tunis d. sc. méd. **16**:345 (Aug.) 1922.
94. Bechet, P. E.: New York M. J. **116**:372 (Oct. 4) 1922.

genital organs were extremely infantile and atrophic. A large part of the trunk and thighs was covered with patches of aggregated red, acuminate papules, with hyperkeratosis of the pilosebaceous follicles. Biopsy made on a lesion on the shoulder showed marked thickening of the corneous layer of the epiderm, particularly at the mouths of the hair follicles, forming plugs. The sweat and sebaceous glands were few in number and small. The patient was given pituitary extract (posterior lobe) in one half grain tablets three times a day. There was marked and progressive improvement in both the eruption and the hypopituitary condition within a few weeks.

Fol and Jaeger[95] report a case of *"creeping disease"* in a girl, 4 years old. On the buttocks, there appeared a reddish stripe, which became longer from day to day. When the child was taken to the hospital a month later, a tortuous line was found, which was disappearing at one end and advancing at the other. There were four zones: (1) a progressive zone, consisting of a simple red line on the skin; (2) a fresh reaction zone, consisting of a narrow central stripe covered with vesicles and passing into an erythematopapulous part; (3) a zone of regression, a brownish stripe with sharp boundaries without signs of inflammation, covered with crusts, and (4) a critical zone of small flat, livid scales. The parasite followed an irregular line and reached the anterior surface of the thigh, and seemed to advance more rapidly in the night, covering from 5 to 10 cm. daily. The parasite could not be isolated from the lesions. Retrogression of the symptoms followed within a short time under the use of disinfectants. Histologic examination of different zones of the affected skin showed that the course of the larva was blocked in skin layers of different depths, often at the boundary of the body of the papilla, but often also in the superficial layer of the epidermis.

Fox[96] recommends the use of mercury in the treatment of flat warts. Mercurous iodid in doses of one fourth grain, three times a day, is given internally. Fox remarks that, from his limited experience with mercury therapy of warts, there is no doubt that, in a certain percentage of cases, successful results can be obtained.

Senear and Fink[97] give an excellent treatise on hydroa vacciniforme seu aestivale, which is an interesting skin condition occurring chiefly in the spring and summer months. The disease usually begins in childhood. In practically all cases, the eruption is confined, at least during

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95. Fol, P. M., and Jaeger, H.: Schweiz. med. Wchnschr. **52**:1011 (Oct. 12) 1922.

96. Fox, Howard: Treatment of Flat Warts by Internal Administration of Mercury, Am. J. Dis. Child. **25**:55 (Jan.) 1923.

97. Senear, F. E., and Fink, H. W.: Hydroa Vacciniforme Seu Aestivale, Arch. Dermat. & Syph. **7**:145 (Feb.) 1923.

its height, to these seasons. March and April are the chief months for the onset of the annual attacks, with recurrences during the spring and summer months, or sometimes through the fall and winter. August and September are usually the latest months in which any considerable eruption is present. The reasons for the seasonal occurrences are obvious. During these months, the luminous intensity of the sun's rays are greatest.

Ehrmann [98] was the first author to study experimentally the effect of light on a patient suffering with hydroa vacciniforme. Using a Finsen light with a blue filter, he exposed parts of the skin normally covered by the clothes and was able to produce typical lesions which resulted in scar formation. Ehrmann concluded that short actinic rays not absorbed by blue glass but absorbed by red glass, acting on persons with an idiosyncrasy for these rays, produce the eruption. This conclusion has been verified several times by other writers, and leaves no doubt of the correctness of Ehrmann's [98] view. Further evidence of the origin from the chemical rays of the sun lies in the observation that, in hydroa vacciniforme, the lesions appear some hours after exposure to the sun's rays.

The question of the etiologic importance of atmospheric factors other than the actinic rays of the sun is still unsettled. In a number of cases, it has been stated that the wind is capable of exciting the eruption, although in these cases the presence also of the actinic rays of the sun could not be entirely ruled out.

The distribution of the eruption in hydroa vacciniforme is on the exposed parts of the body, but it should be understood that the predilection for these parts exists only because they are exposed to the light. It is probable that, in affected persons, the eruption might occur on any part of the cutaneous surface exposed to sufficiently intense sunlight. This has been demonstrated repeatedly, both clinically and experimentally. The parts affected most frequently are the ears, the face, especially the nose and the flush portion of the cheeks, and the dorsal surface of the hands. The cornea may be affected, also the mucous membrane of the mouth, and in one case, the tongue was involved.

The vacciniform type of eruption is the most characteristic form. In this type, erythematous lesions develop first, and on these appear transparent vesicles of a herpetiform character. At times, the lesions begin as hard nodules, which increase peripherally and gradually rise above the level of the skin. They may be single or more or less grouped. They vary from pinhead to pea size, but, through coalescence, they may form bullae. These lesions, if small and superficial, may dry

98. Ehrmann, S.: Arch. f. Dermat. u. Syph. **77**:163, 1905, quoted by Senear: Footnote 97.

up in a day or two, leaving a thin crust, or may rupture and leave a thicker, yellowish crust. The larger and more deeply seated lesions have at first a clear content, which may later become purulent or brownish. The center sinks in and a brownish or black crust, which gradually becomes larger peripherally, forms. At this stage, the lesions resemble closely a vaccination pustule, and like the latter, do not collapse when punctured, as dissepiments give it a multilocular character. In this type, the crust may not be shed for weeks. The lesions as a rule have an areola.

Variations from the characteristic eruption may be of three types. In the first of these, the eruption is of a mild character. The lesions are papulovesicular, fairly superficial and never of the umbilicated type. The duration of the individual lesion is short. In spite of this, and without the aid of trauma or secondary infection, scarring is produced. The second group comprises those cases in which the lesions, covered with a thick yellowish crust, assume an impetiginous form. In several instances, this impetiginization has masked the essential picture, leading to error in diagnosis for a time. In the third form, the eruption is of a severe bullous variety. In many of the vacciniform cases, some bullae are present. This form is often difficult to diagnose, but histologic study of the skin confirms the diagnosis of hydroa vacciniforme.

Local symptoms are usually present. The outbreak is often preceded by sensations of burning or fulness in the affected parts. After the eruption is once established, the patient may suffer itching and occasionally pain, but frequently does not complain of any symptoms. In some cases, the attacks may be ushered in by general symptoms, such as chills, nausea, and at times, vomiting. Malaise and a slight temperature are the symptoms most frequently seen.

Senear and Fink [97] presented a case of hydroa vacciniforme occurring in a schoolboy, 11 years of age. The patient was first seen in July, 1921. The previous year he had a febrile condition, which was suspected of being typhoid fever, lasting from Thanksgiving to December. Shortly after this, he developed an eruption over the buttocks, which at first was thought to be due to some medicine which he had taken. This practically disappeared in about three weeks, but it recurred immediately, and soon healed under local treatment. In March, 1921, he developed an eruption on the ears. A short time later, the face and neck became involved, and there were a few lesions on the arms. This eruption consisted of vesicles, some of which became pustular. The lesions ruptured, became crusted and disappeared in a few weeks leaving small scars. New lesions had appeared in crops from time to time since then, all running the same course. When seen in July, the patient had a number of papulovesicular and pustular lesions in the butterfly area on the face, on the ears, the forearms and the

buttocks. On the back of the hands, there were a number of pinhead size vesicles. The ears, face, back of the neck and backs of the hands showed a number of small white scars, which could scarcely be called vacciniform. The boy spent the remainder of the summer in Virginia, and, by avoiding exposure to the sun, he had been comparatively free from the eruption. He was seen again, March 15, 1922. The mother said that he had had no lesions during the winter but that about a week before he had gone on a "hike" with his Boy Scout company, the day being both sunny and windy. On the following day, the eruption appeared, preceded by itching and burning. It involved only the butterfly area of the face, the ears and the back of the hands. The eruption at this time consisted of pinhead size lesions, which had evidently been vesicular. The crusts were of a clean honey-colored appearance and not adherent. The lesions did not seem sufficiently severe to result in scar formation. No umbilicated lesions had been seen at any time. There was slight burning and itching with the outbreaks, not severe enough to cause scratching of the lesions, so the scarring could not be attributed to trauma.

In the treatment of hydroa vacciniforme, the list of applications used in an attempt to protect the skin is long, but none of them seem to have had any effect. Treatment has been of little avail, although ointments containing quinin or esculin have been reported as of value in some cases.

A CASE OF MENINGITIS DUE TO MICROCOCCUS CATARRHALIS *

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History.—S. J., a Jewish girl, aged 5 years, admitted to the pediatric service at the Boston City Hospital, March 2, 1923, two weeks previously had awakened at night with nausea and vomiting, a sore throat, and a temperature of 100 F. Five or six days before admission, she had a severe headache on the left side, associated with pain in the left ear, and became drowsy. The headache grew progressively worse and was present day and night. No history of convulsions or paralyses was obtained.

Physical Examination.—The child, a well developed and well nourished girl, was irritable and uncooperative. She breathed rapidly, and the face was flushed, the tongue coated, and the pharynx injected. Marked rigidity of the neck was present, with pain on the slightest motion. The Kernig sign was positive. The temperature was elevated, and the pulse and respirations were increased. Examination of the urine was negative. A lumbar puncture was made and a slightly cloudy fluid under increased pressure was obtained, containing 1,500 cells per cubic millimeter, of which 90 per cent. were polymorphonuclear and 10 per cent. mononuclear cells. The globulin was increased. The sugar content was 33.8 mg. per hundred cubic centimeters. Intracellular gram-negative diplococci were found and 30 c.c. of antimeningococcus serum was administered.

Course.—March 3: Lumbar puncture was performed twice and 30 and 25 c.c. of serum injected into the spinal canal.

March 4: Lumbar puncture was again performed twice and 25 and 10 c.c. of serum injected. The fluid was still cloudy, containing 1,620 cells, of which 88 per cent. were polymorphonuclear and 12 per cent. mononuclear. The globulin test remained positive.

March 5: No fluid could be obtained by lumbar puncture.

March 6: The laboratory reported that the organism was not agglutinated by the state antimeningococcus serum. The white cell count was 14,200. The patient's general condition remained about the same.

March 10: Slight improvement was reported, although the evening temperature continued to reach from 103 to 104 F. The white count was 20,000. No lumbar puncture had been attempted since March 5 on account of an area of infected skin on the back.

March 14: The Widal test was reported negative, the patient's general condition remaining about the same.

March 16: A slightly cloudy fluid was obtained, containing 1,350 cells, of which 90 per cent. were polymorphonuclear and 10 per cent. mononuclear. The fluid was cultured and *Micrococcus catarrhalis* was found.[1] The white cell count was 11,900.

March 22: Physical examination disclosed no change in signs, although the patient was losing weight rapidly. The fundi were negative.

March 24: Lumbar puncture yielded an opalescent fluid, under normal pressure, containing 4,250 cells, of which 85 per cent. were polymorphonuclear.

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* From the pediatric service of the Boston City Hospital.

1. The bacteriologic findings are summarized chiefly from work done in the Pathological Laboratory of the Boston City Hospital by Marion E. Lamb. Some of the attempts to agglutinate the organisms with antimeningococcic horse serums were carried out at the Antitoxin and Vaccine Laboratory of the Massachusetts Department of Public Health.

March 30: The fluid contained 3,500 cells, 82 per cent. polymorphonuclear. Stiffness of the neck and a double Kernig sign persisted. The white cell count was 21,550.

April 3: Prolonged coughing spells were noted, with a suggestive whoop.

April 7: The paroxysmal cough was noted as being more severe and associated with vomiting. The patient was much weaker, showing marked loss of weight and turgor. The neurologic signs were unchanged. Opalescent fluid under normal pressure, obtained by lumbar puncture, contained 2,486 cells, of which 78 per cent. were polymorphonuclear and 22 per cent. mononuclear. The globulin test was positive.

April 17: A small amount of fluid was obtained. The sugar content was 45.1 mg. per hundred cubic centimeters. An insufficient amount was obtained for further examination.

April 19: The white count was 68,540.

April 23: The temperature was noted as having been normal for several days. The meningitic signs at this time were subsiding, but the pertussis continued severe and was associated with rapid loss of weight and strength.

May 5: The left ear began to discharge. Vomiting had ceased, but the cough continued. Practically no nourishment was being taken voluntarily and nasal feedings were instituted.

The course of the disease continued unchanged until the death of the patient, May 29, eighty-eight days after admission to the hospital and about 102 days after the onset of symptoms. No necropsy could be obtained.

Dr. Josephine B. Neal of the Bureau of Laboratories of the New York Department of Health, in a personal communication, reports a case of *Micrococcus catarrhalis* meningitis, first seen, Feb. 8, 1922, when the patient was 7 weeks old. Lumbar and ventricular puncture yielded a cloudy yellow fluid, and antimeningococcus serum was given The organism was cultured and found to be *Micrococcus catarrhalis*, and an autogenous vaccine was made and injected intraventricularly. Although some clinical improvement took place, the outcome of the disease was not affected and the infant died the following month.

Two other cases of *Micrococcus catarrhalis* meningitis have been reported by Cassoute and Gibaud [2] and Cot and Robert.[3] In the case reported by Cot and Robert, *Enterococcus* and *Micrococcus catarrhalis* were cultured from the spinal fluid. The meningitis was mild, but, on the thirty-second day, orchitis of the mumps type developed.

A case of this nature is interesting partly from its rarity but more especially on account of the twofold lesson it teaches: (1) it is self-evident that all intracellular gram-negative diplococci found in the spinal fluid are not necessarily meningococci; (2) the spinal fluids from all cases of purulent meningitides should be cultured and agglutination tests made with therapeutic serum in order that a specific serum for the organism may be obtained and used in cases in which the disease is due to the meningococcus.

It is well known that a number of strains of meningococcus exist, grouped according to agglutinin and tropin reactions. At the present

2. Cassoute and Gibaud: Marseille méd. **62**:783, 1920.
3. Cot and Robert: Paris méd. **11**:318 (Oct. 22) 1921.

time, according to Blackfan,[4] the determination of the agglutinin content of the serum is considered, in this country, the most reliable method for the standardization of antimeningococcus serums, as it has been demonstrated that a high agglutination titer is usually accompanied by a strong complement-binding power and a high opsonic index. Serum showing a high agglutination titer for the meningococci isolated from the patient's cerebrospinal fluid, as a rule, gives good therapeutic results. Serum used in treatment should contain antibodies for the two main types of organism and the subtypes.

SUMMARY

A case of *Micrococcus catarrhalis* meningitis, complicated by pertussis and acute otitis media, ended fatally. Three other cases due to the same organism have been collected.

Culturing and testing of the agglutinability of the organism in cases of meningococcus meningitis are important, in order that a specific serum may be used in treatment.

Smears made from the spinal fluid removed at different times and stained by Gram's method consistently showed numerous pus cells, chiefly polymorphonuclear leukocytes, with many intracellular and extracellular gram-negative biscuit-shaped diplococci.

Cultures on blood agar showed abundant growth after eighteen hours' incubation at 37.5 C. The individual colonies were round (from 2 to 5 mm. in diameter), raised, glistening, moist, whitish and somewhat translucent. In the majority of instances, the growth was confluent. There was no hemolysis. The colonies resembled those of the bacilli of the colon group except that they were slightly less translucent. Cultures on plain agar and dextrose agar were identical with those described above. Eighteen-hour plain bouillon cultures showed a general clouding of the medium with a settling out of large numbers of the organisms in the bottom of the tube.

Cultures in Hiss serum (human) water mediums containing 1 per cent. of the various sugars (dextrose, maltose, levulose, saccharose and galactose) all showed growth without the production of acid or gas at the end of forty-eight hours. Smears made from the cultures and stained by Gram's method consistently showed gram-negative diplococci, irregular in size and intensity of staining, and with a tendency to arrange themselves in tetrads.

Attempts to agglutinate salt solution suspensions of the organisms with dilutions (from 1:100 to 1:1,600) of various lots of antimeningococcic horse serum of standard potency were unsuccessful. Likewise, serum obtained from the patient failed to agglutinate the organisms.

Blood cultures taken at different times during the course of the disease were negative.

On the basis of the morphologic, cultural and serologic findings, a bacteriologic diagnosis of *Micrococcus catarrhalis* was made.

270 Commonwealth Avenue.

4. Blackfan, K. D.: Medicine **1**:139 (May) 1922.

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